



# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 142151

**TO:** Shailendra Kumar

**Location:** 5c03 / 5c18

**Tuesday, January 11, 2005**

**Art Unit:** 1621

**Phone:** 272-0640

**Serial Number:** 10 / 701942

**From:** Jan Delaval

**Location:** Biotech-Chem Library

**Rem 1a51**

**Phone:** 272-2504

**jan.delaval@uspto.gov**

Search Notes

Jan Please

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name:

S. Kumar

Examiner #: 69594 Date: 1/10/05

Art Unit: 1621

Phone Number: 2-0640

Serial Number: 101701942

Mail Box and Bldg/Room Location

Results Format Preferred (circle)  PAPER  DISK  E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

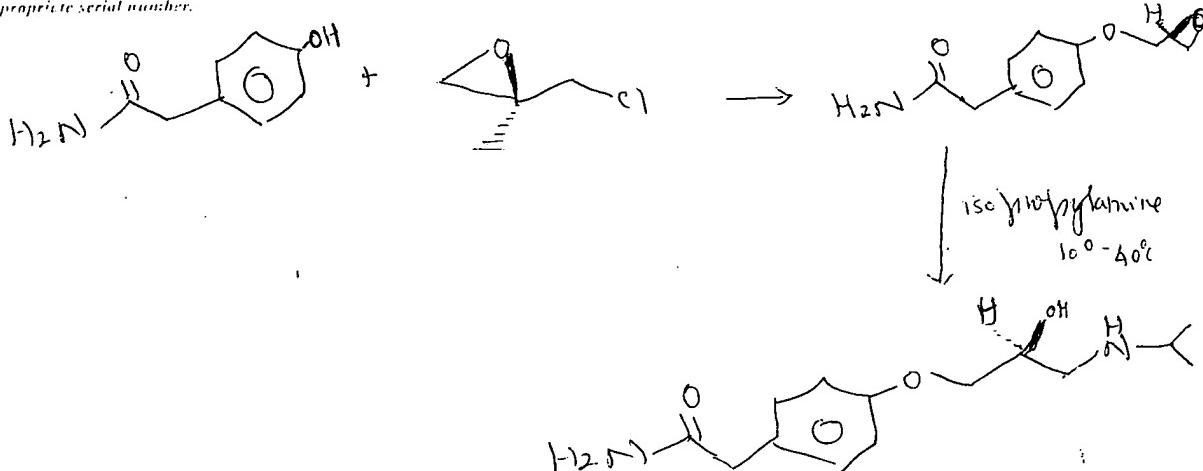
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of invention: Process for producing acetoneol of high optical purity

Inventors (please provide full names): Satish Ramanand Mehta et al.

Earliest Priority Filing Date: 10/30/2003

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.



## STAFF USE ONLY

Searcher: dm

## Type of Search

## Vendors and cost where applicable

Searcher Phone #: 22504

NA Sequence (#)

STN

Searcher Location: \_\_\_\_\_

Structure (#)

Questel/Orbit

Date Searcher Picked Up: 1/10/05

Bibliographic

DRI Link

Date Completed: 1/10/05

Litigation

Lexis/Nexis

Searcher Pre-Review Time: 16:00

Full Text

Sequence System

Searcher Prep Time: 16

Patent Faculty

WWW/Internet

Comments: 745

Other

Other (Specify)

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:19:39 ON 11 JAN 2005
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FILE COVERS 1907 - 11 Jan 2005 VOL 142 ISS 3  
FILE LAST UPDATED: 10 Jan 2005 (20050110/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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(FILE 'HOME' ENTERED AT 10:17:04 ON 11 JAN 2005)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:17:10 ON 11 JAN 2005
E ATENOLOL/CN

L1	1 S E3
	E C14H22N2O3/MF
L2	342 S E3 AND 46.150.18/RID AND 1/NR
L3	18 S L2 AND BENZENEACETAMIDE
L4	12 S L3 AND 2 HYDROXY
L5	11 S L4 AND PROPOXY
L6	7 S L5 AND 4
L7	3 S L6 NOT (D/ELS OR 11C#)
L8	3 S L2 AND ATENOLOL
L9	3 S L1,L7,L8
	SEL RN
L10	37 S E1-E3/CRN
L11	10 S L10 NOT (MXS/CI OR COMPD OR WITH)
	E EPICHLOROHYDRIN/CN
L12	1 S E3
	E C3H5CLO/MF
L13	23 S E3 AND OC2/ES
	SEL RN 12 17 23
L14	3 S E1-E3
L15	3 S L12,L14
	E C11H13NO3/MF
L16	55 S E3 AND 46.150.18/RID AND OC2/ES AND 2/NR
L17	17 S L16 AND 4
L18	5 S L17 AND BENZENEACETAMIDE
L19	3 S L18 NOT D/ELS
	E C8H9NO2/MF
L20	392 S E3 AND 46.150.18/RID AND 1/NR
L21	147 S L20 AND 4
L22	1 S L21 AND BENZENEACETAMIDE
L23	9 S L20 AND BENZENEACETAMIDE
L24	2 S (SODIUM HYDROXIDE OR POTASSIUM HYDROXIDE)/CN

FILE 'HCAPLUS' ENTERED AT 11:12:24 ON 11 JAN 2005

L25 116 S L22  
 L26 15885 S L15  
 L27 32010 S EPICHLOROHYDRIN?  
 L28 35012 S L26,L27  
 L29 58 S L19  
 L30 3162 S L9 OR L11  
 L31 4161 S ATENOLOL  
 L32 4406 S L30,L31  
 L33 19 S L25 AND L28 AND L29 AND L32  
 L34 6 S L33 AND (L24 OR NAOH OR KOH OR (NA OR K OR SODIUM OR POTASSIU  
 L35 1 S L33 AND (QUAT?(L)AMMON?)  
 L36 6 S L34,L35  
 L37 105 S L30 (L) PREP+NT/RL  
 L38 18 S L33 AND L37  
 L39 8366 S (L22 OR L28 OR L19) (L)RACT+NT/RL  
 L40 920 S (L22 OR L28 OR L19) (L)CAT/RL  
 L41 18 S L38 AND L39,L40  
 L42 6 S L36 AND L41  
 L43 13 S L33-L36,L38,L41 NOT L42  
 L44 19 S L42,L43  
 SEL RN

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L45 116 S E1-E116  
 L46 1 S L45 AND L22  
 L47 3 S L45 AND L15  
 L48 3 S L45 AND L19  
 L49 5 S L45 AND L9,L11  
 L50 104 S L45 NOT L46-L49  
 L51 3 S L50 AND IUM  
 L52 3 S L50 AND N N N  
 L53 3 S L50 AND N N  
 L54 3 S L51-L53  
 L55 1 S L45 AND L24

FILE 'HCAPLUS' ENTERED AT 11:19:16 ON 11 JAN 2005

L56 2 S L54 AND L44  
 L57 19 S L44,L56

FILE 'HCAPLUS' ENTERED AT 11:19:39 ON 11 JAN 2005

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L57 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2004:885852 HCAPLUS  
 DN 141:337650  
 ED Entered STN: 26 Oct 2004  
 TI Process for the purification of atenolol  
 IN Datta, Debashish; Muralikrishna, Dantu; Patel, Jayesh Raman  
 PA Lupin Laboratories Ltd., India  
 SO Indian, 21 pp.  
 CODEN: INXXAP  
 DT Patent  
 LA English  
 IC ICM C07C103-26  
 ICS A61K031-165  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 25  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI IN 182584 A 19990508 IN 1996-B0529 19961101  
 PRAI IN 1996-B0529 19961101

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
IN 182584	ICM	C07C103-26
	ICS	A61K031-165

AB A process for purification of atenolol which comprises slurring a crude atenolol base in water and adjusting the pH to 4-8 with a mineral acid at which the crude base dissolves to form a solution, filtering the resulting solution to remove neutral impurities which are insol. in water, treating the aqueous acidic filtrate with activated charcoal to remove the remaining undesired impurities and filtering the charcoal-treated solution and treating with an alkali and separating the atenolol in purified form.

ST atenolol purifn process

IT Charcoal

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)  
 (activated; process for purification of atenolol)

IT 29122-68-7P, Atenolol

RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);  
 PREP (Preparation); USES (Uses)

IT 75-31-0, Isopropylamine, reactions 106-89-8,

Epichlorohydrin, reactions 17194-82-0,  
 p-Hydroxyphenylacetamide

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (process for purification of atenolol)

IT 29122-69-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (process for purification of atenolol)

IT 56392-14-4 61698-76-8 87619-83-8

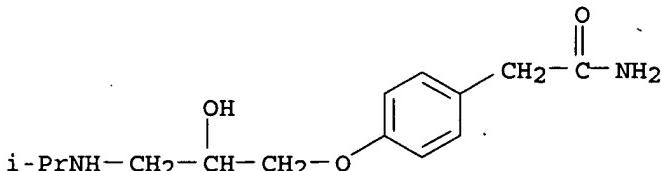
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)  
 (synthetic impurity; process for purification of atenolol)

IT 29122-68-7P, Atenolol

RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);  
 PREP (Preparation); USES (Uses)  
 (process for purification of atenolol)

RN 29122-68-7 HCPLUS

CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)

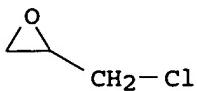


IT 106-89-8, Epichlorohydrin, reactions 17194-82-0  
 , p-Hydroxyphenylacetamide

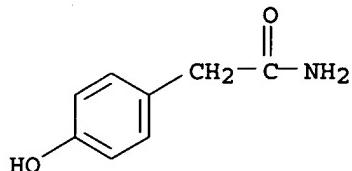
RL: RCT (Reactant); RACT (Reactant or reagent)  
 (process for purification of atenolol)

RN 106-89-8 HCPLUS

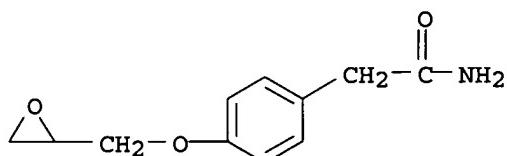
CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



RN 17194-82-0 HCPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



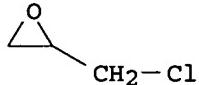
IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (process for purification of atenolol)  
 RN 29122-69-8 HCPLUS  
 CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



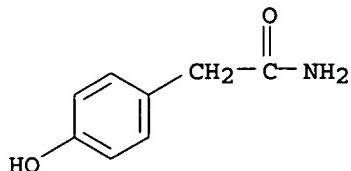
L57 ANSWER 2 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN  
 AN 2000:610971 HCPLUS  
 DN 134:41957  
 ED Entered STN: 05 Sep 2000  
 TI Synthesis of atenolol from benzylcyanide  
 AU Wei, Chang-mei  
 CS Dept. of Chemistry, Huaiyin Normal College, Huaiyin, 223001, Peop. Rep. China  
 SO Huaihai Gongxueyuan Xuebao (2000), 9(2), 36-38  
 CODEN: HGKFX; ISSN: 1008-3499  
 PB Huaihai Gongxueyuan Xuebao Bianjibu  
 DT Journal  
 LA Chinese  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1  
 OS CASREACT 134:41957  
 AB The title antihypertensive was prepared in 7 step in 12.06% yield from benzyl cyanide.  
 ST atenolol prepn antihypertensive  
 IT Antihypertensives  
 (synthesis of atenolol from benzyl cyanide)  
 IT 75-31-0, Isopropylamine, reactions 106-89-8,  
 Epichlorohydrin, reactions 140-29-4, Benzyl cyanide  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of atenolol from benzyl cyanide)  
 IT 104-03-0P 156-38-7P 555-21-5P 1197-55-3P 17194-82-0P  
 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)  
 (synthesis of atenolol from benzyl cyanide)

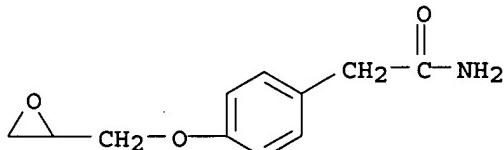
IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of atenolol from benzyl cyanide)  
 IT 106-89-8, Epichlorohydrin, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of atenolol from benzyl cyanide)  
 RN 106-89-8 HCPLUS  
 CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



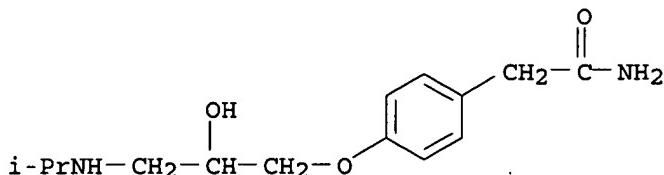
IT 17194-82-0P 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (synthesis of atenolol from benzyl cyanide)  
 RN 17194-82-0 HCPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



RN 29122-69-8 HCPLUS  
 CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of atenolol from benzyl cyanide)  
 RN 29122-68-7 HCPLUS  
 CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)



L57 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1999:785138 HCAPLUS  
 DN 132:122142  
 ED Entered STN: 12 Dec 1999  
 TI CsF in organic synthesis. Regioselective nucleophilic reactions of phenols with oxiranes leading to enantiopure  $\beta$ -blockers  
 AU Kitaori, Kazuhiro; Furukawa, Yoshiro; Yoshimoto, Hiroshi; Otera, Junzo  
 CS Research Laboratories of Daiso Co., Ltd., Amagasaki, 660-0842, Japan  
 SO Tetrahedron (1999), 55(50), 14381-14390  
 CODEN: TETRAB; ISSN: 0040-4020  
 PB Elsevier Science Ltd.  
 DT Journal  
 LA English  
 CC 21-2 (General Organic Chemistry)  
 OS CASREACT 132:122142  
 AB The two modes of the paths in the reaction of oxiranes with phenols are completely controlled by CsF. Glycidyl nosylate undergoes exclusive substitution at the C1 position whereas the ring-opening (C-3 attack) occurs with **epichlorohydrin**, glycidol, and 1,2-epoxyalkanes. These reactions provide convenient access to enantiopure  $\beta$ -blockers.  
 ST nucleophilic reaction phenol oxirane cesium fluoride  
 IT Regiochemistry  
 Ring opening  
 Substitution reaction, nucleophilic  
 (regioselective nucleophilic reactions of phenols with oxiranes in presence of cesium fluoride)  
 IT Epoxides  
 Phenols, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (regioselective nucleophilic reactions of phenols with oxiranes in presence of cesium fluoride)  
 IT 67-56-1, Methanol, reactions 100-51-6, Benzyl alcohol, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (regioselective nucleophilic reactions of phenols or alcs. with oxiranes in presence of cesium fluoride)  
 IT 56552-80-8P 86195-49-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (regioselective nucleophilic reactions of phenols or alcs. with oxiranes in presence of cesium fluoride)  
 IT 13400-13-0, Cesium fluoride  
 RL: CAT (Catalyst use); USES (Uses)  
 (regioselective nucleophilic reactions of phenols with oxiranes in presence of cesium fluoride)  
 IT 90-05-1, 2-Methoxyphenol 95-48-7, reactions 99-76-3, Methyl 4-hydroxybenzoate 100-02-7, reactions 106-41-2, 4-Bromophenol 106-44-5, 4-Methylphenol, reactions 106-48-9, 4-Chlorophenol 108-95-2, Phenol, reactions 123-08-0 150-76-5, 4-Methoxyphenol 767-00-0, 4-Cyanophenol 1126-20-1, 2-Allyloxyphenol 1436-34-6, Butyloxirane 14191-95-8, 4-Cyanomethylphenol 17194-82-0 51594-55-9, (R)-**Epichlorohydrin**, reactions 60456-23-7, (S)-Glycidol 70987-78-9 77495-66-0, (R)-Hexyloxirane 118712-60-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (regioselective nucleophilic reactions of phenols with oxiranes in presence of cesium fluoride)  
 IT 3102-00-9P 4199-10-4P 22972-96-9P 26328-11-0P 52153-43-2P  
**56715-12-9P** 61248-75-7P 66901-82-4P 70987-80-3P  
 71031-03-3P 71048-65-2P 82430-38-4P **93379-54-5P**, (S)-  
**Atenolol** 99103-03-4P 101693-40-7P 112652-61-6P  
 125279-82-5P 129098-55-1P 129098-57-3P 154872-58-9P 154968-43-1P  
 256460-10-3P 256460-11-4P 256460-14-7P 256460-15-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (regioselective nucleophilic reactions of phenols with oxiranes in presence of cesium fluoride)

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Ader, U; Tetrahedron: Asymmetry 1992, V3, P521 HCPLUS
- (2) Cardillo, G; Tetrahedron 1987, V43, P2505 HCPLUS
- (3) Caron, M; J Org Chem 1985, V50, P1557 HCPLUS
- (4) Chen, J; Tetrahedron Lett 1995, V36, P2379 HCPLUS
- (5) Fuji, M; Chem Pharm Bull 1992, V40, P2353 HCPLUS
- (6) Guivis dalsky, P; J Org Chem 1989, V54, P4637 HCPLUS
- (7) Iranpoor, N; Synth Commun 1990, V20, P2789 HCPLUS
- (8) Ishibashi, H; Chem Pharm Bull 1994, V42, P271 HCPLUS
- (9) Ishibashi, H; Tetrahedron Lett 1993, V34, P489 HCPLUS
- (10) Kitaori, K; Chem Pharm Bull 1997, V50, P1557
- (11) Kitaori, K; Synlett 1998, P499 HCPLUS
- (12) Kitaori, K; Tetrahedron Lett 1998, V39, P3173 HCPLUS
- (13) Klunda, J; J Org Chem 1986, V51, P3710
- (14) Klunder, J; J Org Chem 1989, V54, P1295 HCPLUS
- (15) Ko, S; J Org Chem 1986, V51, P5413 HCPLUS
- (16) Ko, S; J Org Chem 1987, V52, P667 HCPLUS
- (17) Mambu, Y; Tetrahedron Lett 1990, V31, P1723
- (18) Martin, V; Tetrahedron Lett 1988, V29, P2701 HCPLUS
- (19) Masaki, Y; Synlett 1993, P847 HCPLUS
- (20) McClure, D; J Am Chem Soc 1979, V101, P3666 HCPLUS
- (21) Moberg, C; Tetrahedron Lett 1992, V33, P21971
- (22) Nelson, W; J Org Chem 1977, V42, P1006 HCPLUS
- (23) Nelson, W; J Org Chem 1978, V43, P3641 HCPLUS
- (24) Otera, J; J Org Chem 1988, V53, P27
- (25) Otera, J; Tetrahedron 1997, V53, P13633 HCPLUS
- (26) Otera, J; Tetrahedron Lett 1985, V26, P3219 HCPLUS
- (27) Posner, G; Tetrahedron Lett 1975, P3597 HCPLUS
- (28) Riego, J; Chem Lett 1986, P1565 HCPLUS
- (29) Sasai, H; Tetrahedron 1994, V50, P12313 HCPLUS
- (30) Sato, T; J Org Chem 1995, V60, P2627 HCPLUS
- (31) Sato, T; Synlett 1995, P336 HCPLUS
- (32) Shoda, S; Chem Lett 1980, P391 HCPLUS
- (33) Smith, J; Synthesis 1984, P629 HCPLUS
- (34) Stinson, S; Chem Eng News 1997, June 2, P28
- (35) Wang, Z; Tetrahedron Lett 1993, V34, P2267 HCPLUS
- (36) Wunsche, K; Tetrahedron: Asymmetry 1996, V7, P2017

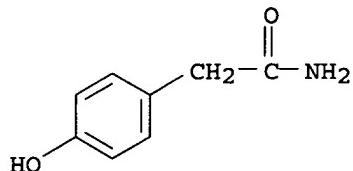
IT 17194-82-0 51594-55-9, (R)-Epichlorohydrin,  
reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(regioselective nucleophilic reactions of phenols with oxiranes in  
presence of cesium fluoride)

RN 17194-82-0 HCPLUS

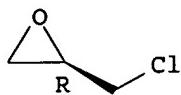
CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



RN 51594-55-9 HCPLUS

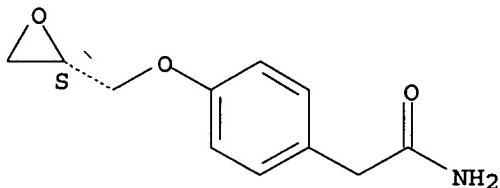
CN Oxirane, (chloromethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



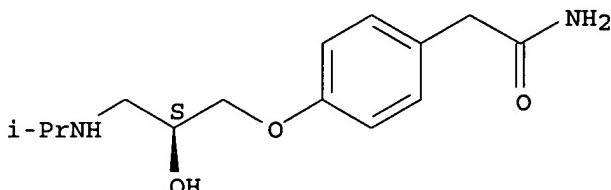
IT 56715-12-9P 93379-54-5P, (S)-Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (regioselective nucleophilic reactions of phenols with oxiranes in presence of cesium fluoride)  
 RN 56715-12-9 HCAPLUS  
 CN Benzeneacetamide, 4-[(2S)-oxiranylmethoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 93379-54-5 HCAPLUS  
 CN Benzeneacetamide, 4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L57 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1999:503559 HCAPLUS  
 DN 131:129738  
 ED Entered STN: 13 Aug 1999  
 TI Improved synthesis of atenolol  
 AU Xu, Bo  
 CS College Pharmaceutical Eng., East China Univ. Sci & Tech, Shanghai, 200237, Peop. Rep. China  
 SO Guangxi Huagong (1999), 28(2), 9-10  
 CODEN: GUHUF2; ISSN: 1003-0840  
 PB Guangxi Huagong Bianjibu  
 DT Journal  
 LA Chinese  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 AB Atenolol was prepared in 2 steps from 4-hydroxyphenylacetamide and epichlorohydrin.  
 ST atenolol prep  
 IT 75-31-0, Isopropylamine, reactions 106-89-8,  
 Epichlorohydrin, reactions 17194-82-0,  
 4-Hydroxyphenylacetamide  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of atenolol)

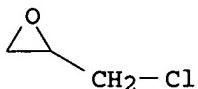
IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (synthesis of atenolol)

IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of atenolol)

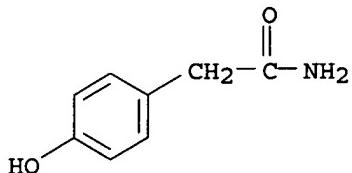
IT 106-89-8, Epichlorohydrin, reactions 17194-82-0  
 , 4-Hydroxyphenylacetamide  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of atenolol)

RN 106-89-8 HCPLUS

CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



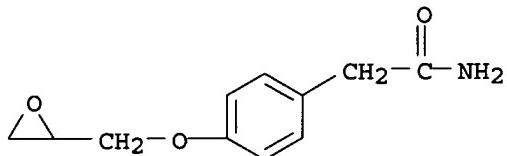
RN 17194-82-0 HCPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (synthesis of atenolol)

RN 29122-69-8 HCPLUS

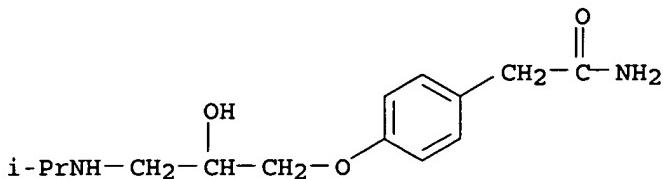
CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of atenolol)

RN 29122-68-7 HCPLUS

CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)



L57 ANSWER 5 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN  
 AN 1998:446687 HCPLUS  
 DN 129:54146  
 ED Entered STN: 20 Jul 1998  
 TI A Synthesis of Atenolol Using a Nitrile Hydration Catalyst  
 AU Akisanya, Joseph; Parkins, Adrian W.; Steed, Jonathan W.  
 CS Department of Chemistry, King's College London, London, WC2R 2LS, UK  
 SO Organic Process Research & Development (1998), 2(4), 274-276  
 CODEN: OPRDFK; ISSN: 1083-6160  
 PB American Chemical Society  
 DT Journal  
 LA English  
 CC 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 AB The synthesis of **atenolol** is described using a platinum containing homogeneous catalyst for the conversion of a nitrile to an amide. The catalytic reaction may be employed as the final step in the synthesis or in the preparation of the intermediate 4-hydroxyphenylacetamide. The structure of the nitrile intermediate, 1-(4'-cyanomethylphenoxy)-2-hydroxy-3-isopropylaminopropane, has been determined by X-ray crystallog.  
 ST **atenolol** prep catalyst  
 IT Catalysts  
     (nitrile hydration; synthesis of **atenolol** using a nitrile hydration catalyst)  
 IT Crystallography  
     (synthesis and crystal structure data of **atenolol** using a nitrile hydration catalyst)  
 IT 29277-73-4P  
     RL: SPN (Synthetic preparation); PREP (Preparation)  
         (synthesis and crystal structure data of **atenolol** using a nitrile hydration catalyst)  
 IT 173416-05-2  
     RL: CAT (Catalyst use); USES (Uses)  
         (synthesis of **atenolol** using a nitrile hydration catalyst)  
 IT 75-31-0, 2-Propanamine, reactions 106-89-8, reactions  
**17194-82-0**  
     RL: RCT (Reactant); RACT (Reactant or reagent)  
         (synthesis of **atenolol** using a nitrile hydration catalyst)  
 IT 14191-95-8P 29122-69-8P 35198-42-6P  
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
         (Preparation); RACT (Reactant or reagent)  
         (synthesis of **atenolol** using a nitrile hydration catalyst)  
 IT 29122-68-7P  
     RL: SPN (Synthetic preparation); PREP (Preparation)  
         (synthesis of **atenolol** using a nitrile hydration catalyst)  
 RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Barbour, L; RES2INS 1995  
 (2) Barrett, A; DE 2007751 1974 HCPLUS  
 (3) Barrett, A; US 3836671 1974 HCPLUS  
 (4) Bevinakatti, H; J Org Chem 1992, V57, P6003 HCPLUS  
 (5) Eckart, R; Pharmazie 1975, V30, P633  
 (6) Ghaffar, T; Tetrahedron Lett 1995, V36, P8657 HCPLUS

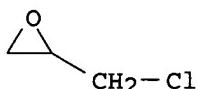
- (7) Kleidernigg, O; Chirality 1994, V6, P411 HCPLUS  
 (8) Le Count, D; Chronicles of Drug Discovery 1982, V1, P113 HCPLUS  
 (9) Liler, M; J Chem Soc 1958, P1084 HCPLUS  
 (10) March, J; Advanced Organic Chemistry, 4th ed 1992, P391  
 (11) Matsuoka, K; US 5386056 HCPLUS  
 (12) Matsuoka, K; WO 9323372 HCPLUS  
 (13) Otwinowski, Z; Methods Enzymol 1996, V276, P307  
 (14) O'Connor, C; Quart Re 1970, V24, P553 HCPLUS  
 (15) Payne, G; J Org Chem 1962, V27, P3819 HCPLUS  
 (16) Rabinovitch, B; Can J Res 1942, V20B, P221 HCPLUS  
 (17) Ravindranathan, M; J Org Chem 1982, V47, P4812 HCPLUS  
 (18) Rietzel, C; GB 2155923 A 1985 HCPLUS  
 (19) Rietzel, C; BE 901850 1985 HCPLUS  
 (20) Rosenberg, H; GB 2212801 A 1989 HCPLUS  
 (21) Salkowski, H; Chem Ber 1889, V22, P2137  
 (22) Schwartz, M; J Org Chem 1976, V41, P2502 HCPLUS  
 (23) Sheldrick, G; SHELXL-97 1997  
 (24) Sugai, T; Biosci Biotech Biochem 1997, V61, P1419 HCPLUS  
 (25) The Cambridge Crystallographic Data Centre; teched@chemcrys.cam.ac.uk  
 (26) Zil'berman, E; Russ Chem Re 1984, V53, P900

IT 106-89-8, reactions 17194-82-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of atenolol using a nitrile hydration catalyst)

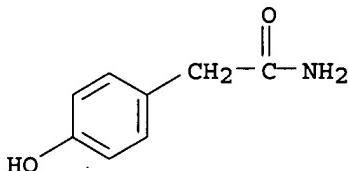
RN 106-89-8 HCPLUS

CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



RN 17194-82-0 HCPLUS

CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)

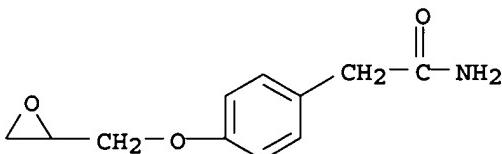


IT 29122-69-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (synthesis of atenolol using a nitrile hydration catalyst)

RN 29122-69-8 HCPLUS

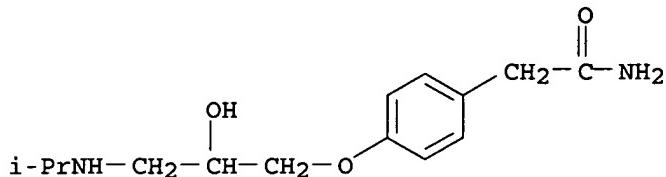
CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of atenolol using a nitrile hydration catalyst)

RN 29122-68-7 HCAPLUS  
 CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)



L57 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1997:141773 HCAPLUS  
 DN 126:225082  
 ED Entered STN: 05 Mar 1997  
 TI A practical synthesis of optically active **atenolol** from chiral **epichlorohydrin**  
 AU Kitaori, Kazuhiro; Takehira, Yoshikazu; Furukawa, Yoshiro; Yoshimoto, Hiroshi; Otera, Junzo  
 CS Res. Labs. Daiso Co., Ltd., Amagasaki, 660, Japan  
 SO Chemical & Pharmaceutical Bulletin (1997), 45(2), 412-414  
 CODEN: CPBTAL; ISSN: 0009-2363  
 PB Pharmaceutical Society of Japan  
 DT Journal  
 LA English  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 AB The synthesis of (R)-**atenolol** and (S)-**atenolol** was achieved in two steps starting from 4-hydroxybenzeneacetamide. Both enantiomers of 4-(oxiranylmethoxy)benzeneacetamide were synthesized from 4-hydroxybenzeneacetamide and (R)- and (S)-**epichlorohydrin** using an alkali metal hydroxide and/or BTA (benzyltrimethylammonium chloride), resp. Subsequent treatment of the epoxide with isopropylamine afforded **atenolol** with excellent enantiomeric excess (>98% ee).  
 ST **atenolol** asym synthesis; oxiranylmethoxy benzeneacetamide prepn  
**atenolol** intermediate  
 IT Asymmetric synthesis and induction  
 (asym. synthesis **atenolol**)  
 IT 17194-82-0, 4-Hydroxybenzeneacetamide 51594-55-9, (R)-  
**Epichlorohydrin**, reactions 67843-74-7, (S)-  
**Epichlorohydrin**, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (asym. synthesis **atenolol**)  
 IT 56715-12-9P, (S)-4-(Oxiranylmethoxy)benzeneacetamide  
 136259-70-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (asym. synthesis **atenolol**)  
 IT 56715-13-0P, (R)-**Atenolol** 93379-54-5P, (S)-  
**Atenolol**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (asym. synthesis **atenolol**)  
 RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
 (1) Akiyama, A; CHEMTECH 1988, V18, P640  
 (2) Anon; US 3663607 1972 HCAPLUS  
 (3) Anon; US 3836671 1974 HCAPLUS  
 (4) Anon; 1975 HCAPLUS  
 (5) Anon; US 3934032 1976 HCAPLUS  
 (6) Anon; Barclays de Zoete Wedd Research Report 1991, V6(2), P22

- (7) Bevinakatti, H; J Org Chem 1992, V57, P6003 HCPLUS  
 (8) Borman, S; Chem Eng News 1990, V28, P9  
 (9) Chen, C; Angew Chem, Int Ed Engl 1989, V28, P695  
 (10) Deutsch, D; CHEMTECH 1991, V21, P157 HCPLUS  
 (11) Howe, R; Nature (London) 1966, V210, P1336 HCPLUS  
 (12) Kasai, N; Agric Biol Chem 1990, V54, P3158  
 (13) Kasai, N; J Ind Microbiol 1992, V10, P37 HCPLUS  
 (14) Kasai, N; J Ind Microbiol 1992, V9, P97 HCPLUS  
 (15) Klibanov, A; Acc Chem Res 1990, V23, P114 HCPLUS  
 (16) Margolin, A; CHEMTECH 1991, V21, P160 HCPLUS  
 (17) Nelson, W; J Org Chem 1977, V42, P1006 HCPLUS  
 (18) Nelson, W; J Org Chem 1978, V43, P3641 HCPLUS  
 (19) Pearson, A; Chem Eng News 1991, V71, P16  
 (20) Pearson, A; J Pharmacol Exp Ther 1989, V250, P759 HCPLUS  
 (21) Wong, C; Science 1989, V244, P1145 HCPLUS  
 (22) Yamada, H; Angew Chem, Int Ed Engl 1988, V27, P622

IT 17194-82-0, 4-Hydroxybenzeneacetamide 51594-55-9, (R)-

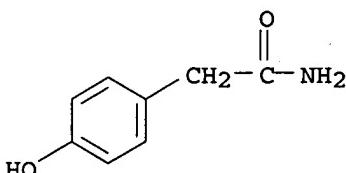
Epichlorohydrin, reactions 67843-74-7, (S)-

Epichlorohydrin, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (asym. synthesis atenolol)

RN 17194-82-0 HCPLUS

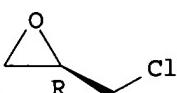
CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



RN 51594-55-9 HCPLUS

CN Oxirane, (chloromethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 67843-74-7 HCPLUS

CN Oxirane, (chloromethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



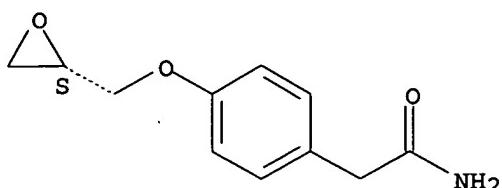
IT 56715-12-9P, (S)-4-(Oxiranylmethoxy)benzeneacetamide  
 136259-70-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (asym. synthesis atenolol)

RN 56715-12-9 HCPLUS

CN Benzeneacetamide, 4-[(2S)-oxiranylmethoxy]- (9CI) (CA INDEX NAME)

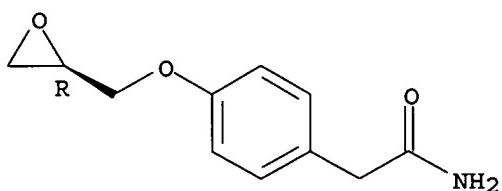
Absolute stereochemistry. Rotation (+).



RN 136259-70-6 HCPLUS

CN Benzeneacetamide, 4-(oxiranylmethoxy)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



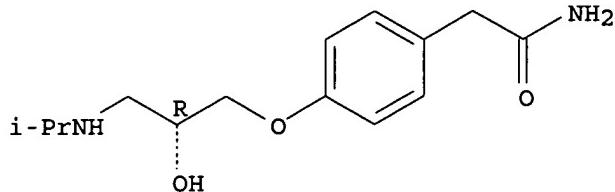
IT 56715-13-0P, (R)-Atenolol 93379-54-5P, (S)-

**Atenolol**RL: SPN (Synthetic preparation); PREP (Preparation)  
(asym. synthesis atenolol)

RN 56715-13-0 HCPLUS

CN Benzeneacetamide, 4-[(2R)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
(9CI) (CA INDEX NAME)

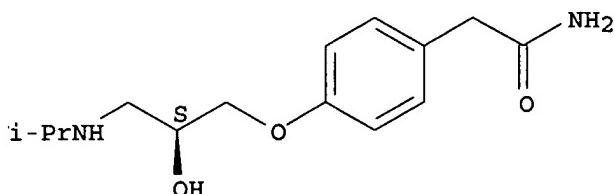
Absolute stereochemistry. Rotation (+).



RN 93379-54-5 HCPLUS

CN Benzeneacetamide, 4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



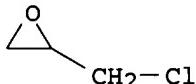
L57 ANSWER 7 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN

AN 1996:482631 HCPLUS

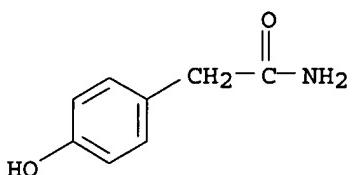
DN 125:167503

ED Entered STN: 14 Aug 1996

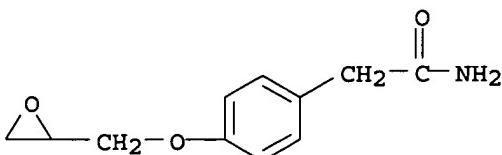
TI Synthesis of atenolol  
 AU Cui, Yanxia; Jiang, Weiguo; Li, Shufen  
 CS Res. Inst. Northeast Gen. Pharmaceutical Factory, Shenyang, 110026, Peop. Rep. China  
 SO Zhongguo Yaowu Huaxue Zazhi (1996), 6(1), 62-63  
 CODEN: ZYHZEF; ISSN: 1005-0108  
 PB Zhongguo Yaowu Huaxue Zazhi Bianjibu  
 DT Journal  
 LA Chinese  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 AB Atenolol was prepared in 2 steps in 52.8% overall yield by etherification of 4-hydroxyphenylacetamide with epichlorohydrin followed by amination with isopropylamine.  
 ST atenolol prep  
 IT 75-31-0, Isopropylamine, reactions 106-89-8,  
 Epichlorohydrin, reactions 17194-82-0, p-Hydroxy phenylacetamide 29122-69-8, Benzeneacetamide, 4-(oxiranylmethoxy)-  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of atenolol)  
 IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (synthesis of atenolol)  
 IT 106-89-8, Epichlorohydrin, reactions 17194-82-0  
 , p-Hydroxy phenylacetamide 29122-69-8, Benzeneacetamide, 4-(oxiranylmethoxy)-  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (synthesis of atenolol)  
 RN 106-89-8 HCPLUS  
 CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



RN 17194-82-0 HCPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



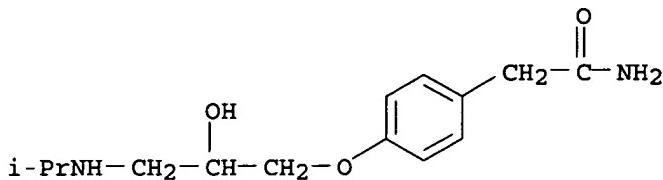
RN 29122-69-8 HCPLUS  
 CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis of atenolol)

RN 29122-68-7 HCPLUS  
 CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)



L57 ANSWER 8 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN

AN 1994:298454 HCPLUS

DN 120:298454

ED Entered STN: 11 Jun 1994

TI Phase transfer catalytic process for preparing intermediates of atenolol, propranolol, and their derivatives

IN Jang, Shyue Ming; Shieh, Tian Shy

PA Industrial Technology Research Institute, Taiwan

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM C07D301-28

ICS C07D303-23; C07C041-03; C07C043-205

NCL 549517000

CC 27-2 (Heterocyclic Compounds (One Hetero Atom))

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5290958	A	19940301	US 1993-33047	19930818
	GB 2276167	A1	19940921	GB 1993-12267	19930615
	GB 2276167	B2	19951213		
PRAI	US 1993-33047	A	19930818		

CLASS

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

US 5290958	ICM	C07D301-28
	ICS	C07D303-23; C07C041-03; C07C043-205
	NCL	549517000

GB 2276167 ECLA C07C041/16; C07D303/22B

OS MARPAT 120:298454

AB The title process comprises O-alkylation of 4-(H<sub>2</sub>NOCH<sub>2</sub>C)C<sub>6</sub>H<sub>4</sub>OH and α-naphthol by epichlorohydrin in the presence of R<sub>1</sub>R<sub>2</sub>R<sub>3</sub>R<sub>4</sub>NX or (R<sub>5</sub>)<sub>3</sub>NHX (1 of R<sub>1</sub>-R<sub>4</sub> = C<sub>9</sub>-20alkyl and the remaining R<sub>1</sub>-R<sub>5</sub> = C<sub>1</sub>-20alkyl; X = halo) to give the corresponding epoxides and halohydrins.

ST atenolol propranolol intermediate; phenol naphthol etherification epichlorohydrin catalyst

IT 106-89-8, Epichlorohydrin, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (O-alkylation of hydroxyphenylacetamide by, in preparation of atenolol intermediate, catalysts for)

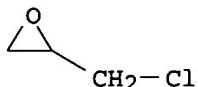
IT 17194-82-0, 4-Hydroxyphenylacetamide

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (O-alkylation of, in preparation of atenolol intermediate, catalysts for)

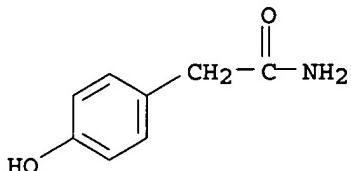
IT 90-15-3, α-Naphthol

RL: RCT (Reactant); RACT (Reactant or reagent)

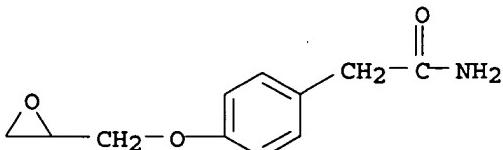
(O-alkylation of, in preparation of propranolol intermediate, catalysts for)  
IT 29122-69-8P 115538-83-5P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as atenolol intermediate, method for)  
IT 2461-42-9P 20133-93-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as propranolol intermediate, method for)  
IT 525-66-6P, Propranolol 29122-68-7P, Atenolol  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, method for)  
IT 75-31-0, Isopropylamine, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, in preparation of atenolol)  
IT 106-89-8, Epichlorohydrin, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(O-alkylation of hydroxyphenylacetamide by, in preparation of  
atenolol intermediate, catalysts for)  
RN 106-89-8 HCPLUS  
CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



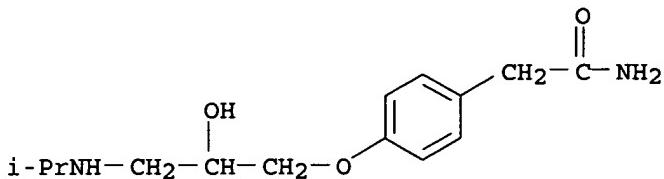
IT 17194-82-0, 4-Hydroxyphenylacetamide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(O-alkylation of, in preparation of atenolol intermediate,  
catalysts for)  
RN 17194-82-0 HCPLUS  
CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



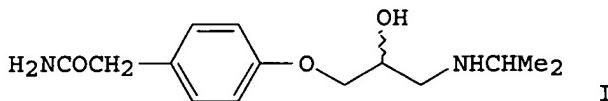
IT 29122-69-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as atenolol intermediate, method for)  
RN 29122-69-8 HCPLUS  
CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P, Atenolol  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, method for)  
RN 29122-68-7 HCPLUS  
CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
(CA INDEX NAME)



L57 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1992:633552 HCAPLUS  
 DN 117:233552  
 ED Entered STN: 13 Dec 1992  
 TI Lipase catalysis in organic solvents. Application to the synthesis of (R)- and (S)-atenolol  
 AU Bevinakatti, H. S.; Banerji, A. A.  
 CS Alchemie Res. Cent., Thane, 400601, India  
 SO Journal of Organic Chemistry (1992), 57(22), 6003-5  
 CODEN: JOCEAH; ISSN: 0022-3263  
 DT Journal  
 LA English  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 Section cross-reference(s): 1, 7  
 GI



AB Stereoselective synthesis of (R)- and (S)-atenolol I was achieved in five steps starting from p-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>H. Lipase from Pseudomonas cepacia showed excellent selectivity toward kinetic resolution of key intermediates p-ClCH<sub>2</sub>CH(OR)CH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>Bu (R = H, Ac).  
 ST atenolol stereoselective synthesis; lipase resoln  
 atenolol intermediate  
 IT Pseudomonas cepacia  
     (lipase from, as catalyst in acylation of (chlorohydroxypropoxy)phenylacetate in synthesis of atenolol)  
 IT 75-31-0, Isopropylamine, reactions  
     RL: RCT (Reactant); RACT (Reactant or reagent)  
     (amination by, of (chlorohydroxypropoxyphenyl)acetate, in synthesis of atenolol)  
 IT 71-36-3, 1-Butanol, reactions  
     RL: RCT (Reactant); RACT (Reactant or reagent)  
     (esterification by, of hydroxyphenylacetic acid)  
 IT 156-38-7, p-Hydroxyphenylacetic acid  
     RL: RCT (Reactant); RACT (Reactant or reagent)  
     (esterification of, by butanol)  
 IT 29122-69-8P 115538-83-5P  
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
     (Preparation); RACT (Reactant or reagent)  
     (preparation and acetylation of)  
 IT 143925-25-1P 143925-26-2P  
     RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and conversion to atenolol)

IT 143925-23-9P 143925-24-0P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and kinetic resolution of)

IT 144015-97-4P 144015-98-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and lipase-catalyzed acylation of)

IT 144017-03-8P 144017-04-9P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and lipase-catalyzed deacylation of)

IT 79419-46-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and substitution of, by epichlorohydrin)

IT 143925-21-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 56715-13-0P, (R)-Atenolol 93379-54-5P, (S)-  
**Atenolol**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, by lipase catalyzed kinetic resolution from  
 hydroxyphenylacetic acid)

IT 143925-22-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation, chlorination, and acetylation of)

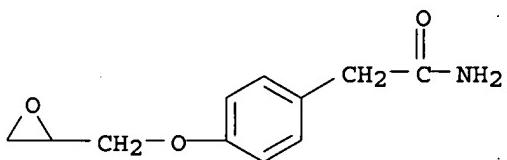
IT 106-89-8, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (substitution by, of hydroxyphenylacetic acid and its amide)

IT 17194-82-0, p-Hydroxyphenylacetamide  
 RL: PROC (Process)  
 (substitution of, by epichlorohydrin)

IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and acetylation of)

RN 29122-69-8 HCPLUS

CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)

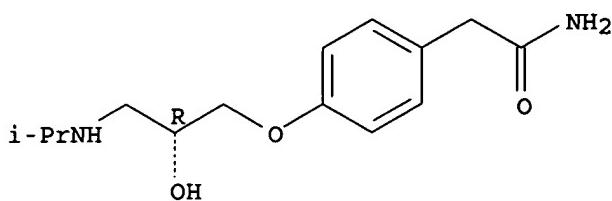


IT 56715-13-0P, (R)-Atenolol 93379-54-5P, (S)-  
**Atenolol**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, by lipase catalyzed kinetic resolution from  
 hydroxyphenylacetic acid)

RN 56715-13-0 HCPLUS

CN Benzeneacetamide, 4-[*(2R)*-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
 (9CI) (CA INDEX NAME)

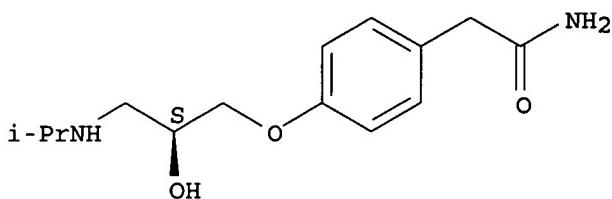
Absolute stereochemistry. Rotation (+).



RN 93379-54-5 HCAPLUS

CN Benzeneacetamide, 4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

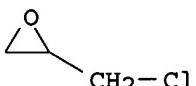


IT 106-89-8, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
(substitution by, of hydroxyphenylacetic acid and its amide)

RN 106-89-8 HCAPLUS

CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)

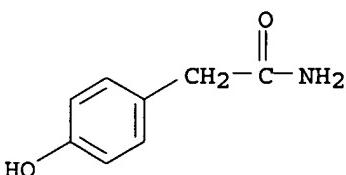


IT 17194-82-0, p-Hydroxyphenylacetamide

RL: PROC (Process)  
(substitution of, by epichlorohydrin)

RN 17194-82-0 HCAPLUS

CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



L57 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1992:612160 HCAPLUS

DN 117:212160

ED Entered STN: 28 Nov 1992

TI Preparation of optically active atenolol and its intermediates

IN Takehira, Kiwa; Saraumi, Nobuaki; Kitaori, Kazuhiro

PA Daiso Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DT Patent

LA Japanese  
 IC ICM C07D301-28  
 ICA A61K031-16; B01J031-02; C07B053-00; C07B061-00; C07D303-22  
 CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 04198175	A2	19920717	JP 1990-331091	19901128
	JP 06037482	B4	19940518		
PRAI	JP 1990-331091		19901128		

## CLASS

	PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
	JP 04198175	ICM	C07D301-28
		ICA	A61K031-16; B01J031-02; C07B053-00; C07B061-00; C07D303-22

OS CASREACT 117:212160

AB H<sub>2</sub>NCOCH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OR-p (II; R = glycidyl) is prepared by treating H<sub>2</sub>NCOCH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OH-p (III) with optically active epichlorohydrin (IV) using alkali hydroxides (A) at equivalent ratio of A/III 1-1.5 in H<sub>2</sub>O-containing solvents in the presence of R<sub>1</sub>R<sub>2</sub>R<sub>3</sub>R<sub>4</sub>N+X- (R<sub>1</sub>-R<sub>4</sub> = C<sub>1</sub>-16 alkyl, alkenyl, aralkyl, aryl; X = Cl, Br, HSO<sub>4</sub>, OH, iodine). Optically active atenolol is prepared by treating II with Me<sub>2</sub>CHNH<sub>2</sub>. An aqueous (R)-(-)-IV was treated dropwise with a mixture of III (35.7 g), benzyltrimethylammonium chloride, and NaOH (9.44 g) in H<sub>2</sub>O at 5° over 1 h, stirred at 5° for 51 h, neutralization by HCl, the suspension was treated added into Me<sub>2</sub>CHNH<sub>2</sub> at 10° over 1 h, then stirred at 20° for 3.5 h to give 72.2% (S)-(-)-atenolol of 94.8% e.e.

ST atenolol prep; hydroxyphenylacetamide etherification  
 epichlorohydrin; isopropylamine ring cleavage  
 glycidyloxyphenylacetamide

IT 51594-55-9, (R)-(-)-Epichlorohydrin, reactions  
 67843-74-7, (S)-(+)-Epichlorohydrin, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (etherification by, of hydroxyphenylacetamide)

IT 17194-82-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (etherification of, by optically active epichlorohydrin)

IT 1310-73-2, Sodium hydroxide, uses  
 1643-19-2, Tetra-n-butylammonium bromide  
 RL: USES (Uses)  
 (in etherification of hydroxyhenylacetamide by epichlorohydrin )

IT 56-93-9, Benzyltrimethylammonium chloride  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in etherification of hydroxyhenylacetamide by epichlorohydrin )

IT 56715-12-9P 136259-70-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and ring cleavage of, by isopropylamine)

IT 56715-13-0P, (R)-(+)-Atenolol 93379-54-5P,  
 (S)-(-)-Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

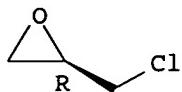
IT 75-31-0, Isopropylamine, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (ring cleavage by, of glycidyloxyphenylacetamide)

IT 51594-55-9, (R)-(-)-Epichlorohydrin, reactions  
 67843-74-7, (S)-(+)-Epichlorohydrin, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (etherification by, of hydroxyphenylacetamide)

RN 51594-55-9 HCPLUS

CN Oxirane, (chloromethyl)-, (2R)- (9CI) (CA INDEX NAME)

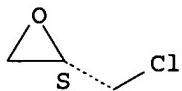
Absolute stereochemistry. Rotation (-).



RN 67843-74-7 HCPLUS

CN Oxirane, (chloromethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

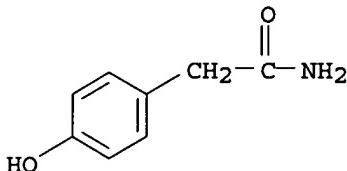


IT 17194-82-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification of, by optically active epichlorohydrin)

RN 17194-82-0 HCPLUS

CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



IT 1310-73-2, Sodium hydroxide, uses

1643-19-2, Tetra-n-butylammonium bromide

RL: USES (Uses)

(in etherification of hydroxyhenylacetamide by epichlorohydrin  
)

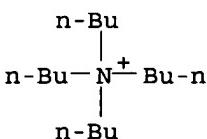
RN 1310-73-2 HCPLUS

CN Sodium hydroxide (Na(OH)) (9CI) (CA INDEX NAME)

Na—OH

RN 1643-19-2 HCPLUS

CN 1-Butanaminium, N,N,N-tributyl-, bromide (9CI) (CA INDEX NAME)



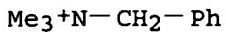
● Br<sup>-</sup>

IT 56-93-9, Benzyltrimethylammonium chloride

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (in etherification of hydroxyhenylacetamide by epichlorohydrin  
 )

RN 56-93-9 HCPLUS

CN Benzenemethanaminium, N,N,N-trimethyl-, chloride (9CI) (CA INDEX NAME)



● Cl<sup>-</sup>

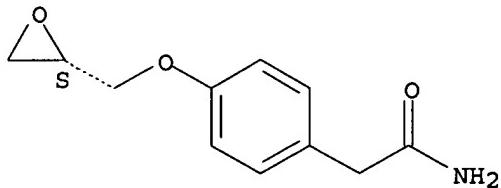
IT 56715-12-9P 136259-70-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and ring cleavage of, by isopropylamine)

RN 56715-12-9 HCPLUS

CN Benzeneacetamide, 4-[(2S)-oxiranylmethoxy]- (9CI) (CA INDEX NAME)

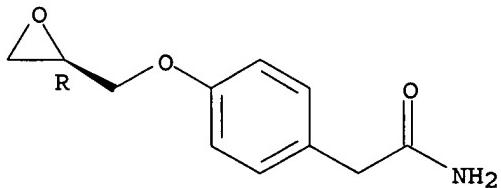
Absolute stereochemistry. Rotation (+).



RN 136259-70-6 HCPLUS

CN Benzeneacetamide, 4-(oxiranylmethoxy)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



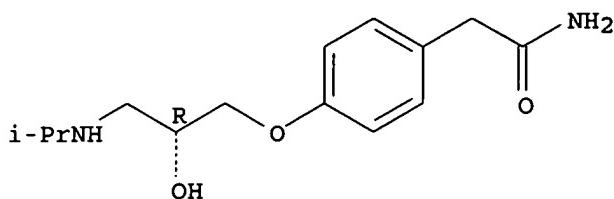
IT 56715-13-0P, (R)-(+)-Atenolol 93379-54-5P,  
 (S)-(-)-Atenolol

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 56715-13-0 HCPLUS

CN Benzeneacetamide, 4-[(2R)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI) (CA INDEX NAME)

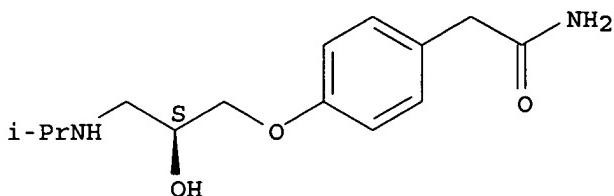
Absolute stereochemistry. Rotation (+).



RN 93379-54-5 HCPLUS

CN Benzeneacetamide, 4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L57 ANSWER 11 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN

AN 1991:558739 HCPLUS

DN 115:158739

ED Entered STN: 18 Oct 1991

TI Manufacture of optically active atenolol and its intermediates

IN Takehira, Kiwa

PA Daiso Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM C07C235-34

ICS C07D301-28; C07D303-22

ICA C07B053-00

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
Section cross-reference(s): 1

FAN.CNT 1

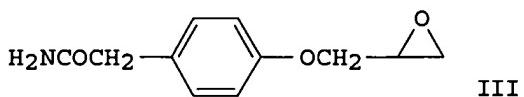
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 03077856	A2	19910403	JP 1989-213148	19890818
	JP 06037449	B4	19940518		
PRAI	JP 1989-213148		19890818		

CLASS

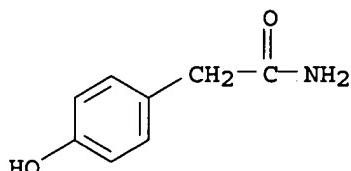
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 03077856	ICM C07C235-34 ICS C07D301-28; C07D303-22 ICA C07B053-00	

OS CASREACT 115:158739

GI



- AB Title compound (I), useful for antihypertensives, is prepared by treating p-hydroxyphenylacetamide (II) with optically active **epichlorohydrin** in a water-containing solvent in the presence of 1-1.5 equivalent alkali metal hydroxide per 1 equivalent **epichlorohydrin** at 0-45° to give III, for example, in pharmacol. active S-form, recrystg. III from an organic solvent if necessary, and treating III with isopropylamine. Thus, treating II with R-(-)-**epichlorohydrin** in aqueous NaOH at 3° to room temperature gave 64% S-(+)-III, which was refluxed with isopropylamine in MeOH to give 89% S-(-)-**atenolol** with optical purity 93%. The purity was improved to 98.3% when S-(+)-III was recrystd. from MeOH before the reaction with isopropylamine.
- ST optically active **atenolol** antihypertensive manuf;  
**epichlorohydrin** hydroxyphenylacetamide etherification;  
isopropylamine addn hydroxyphenylacetamide glycidyl ether
- IT Antihypertensives  
(atenolol, intermediate for, optically active hydroxyphenylacetamide glycidyl ether as)
- IT Etherification  
(hydroxyphenylacetamide with optically active **epichlorohydrin**)
- . IT Addition reaction  
(of optically active hydroxyphenylacetamide glycidyl ether with isopropylamine)
- IT 75-31-0, Isopropylamine, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(addition of, with optically active hydroxyphenylacetamide glycidyl ether)
- IT 17194-82-0, p-Hydroxyphenylacetamide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification of, with optically active **epichlorohydrin**)
- IT 51594-55-9, R-(-)-Epichlorohydrin, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification with, of hydroxyphenylacetamide)
- IT 67843-74-7, S-(+)-Epichlorohydrin, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification with, of hydroxyphenylacetamide)
- IT 56715-12-9P 136259-70-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and addition of, with isopropylamine)
- IT 56715-13-0P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)
- IT 93379-54-5P, S-(-)-Atenolol  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, for antihypertensive)
- IT 17194-82-0, p-Hydroxyphenylacetamide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification of, with optically active **epichlorohydrin**)
- RN 17194-82-0 HCPLUS
- CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



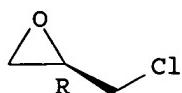
IT 51594-55-9, R-(-)-Epichlorohydrin, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (etherification with, of hydroxyphenylacetamide)

RN 51594-55-9 HCPLUS

CN Oxirane, (chloromethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 67843-74-7, S-(+)-Epichlorohydrin, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
 (etherification with, of hydroxyphenylacetamide)

RN 67843-74-7 HCPLUS

CN Oxirane, (chloromethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



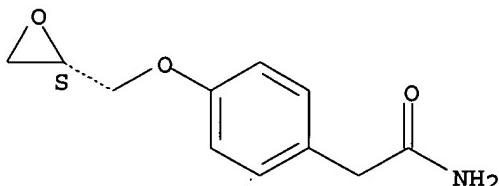
IT 56715-12-9P 136259-70-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and addition of, with isopropylamine)

RN 56715-12-9 HCPLUS

CN Benzeneacetamide, 4-[(2S)-oxiranylmethoxy]- (9CI) (CA INDEX NAME)

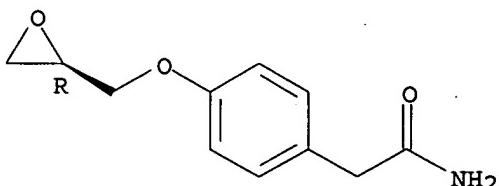
Absolute stereochemistry. Rotation (+).



RN 136259-70-6 HCPLUS

CN Benzeneacetamide, 4-(oxiranylmethoxy)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



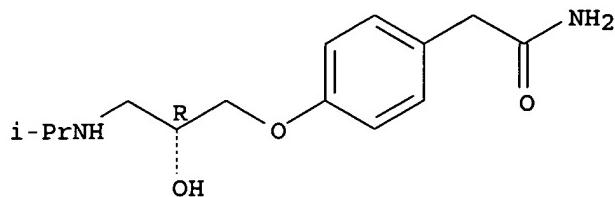
IT 56715-13-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 56715-13-0 HCPLUS

CN Benzeneacetamide, 4-[(2R)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



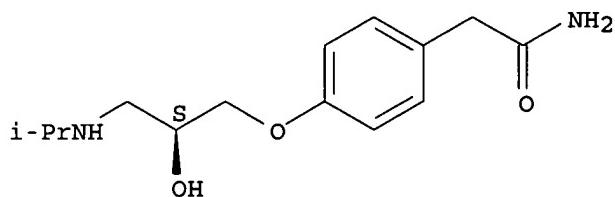
IT 93379-54-5P, S-(-)-Atenolol

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, for antihypertensive)

RN 93379-54-5 HCPLUS

CN Benzeneacetamide, 4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L57 ANSWER 12 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN

AN 1991:558705 HCPLUS

DN 115:158705

ED Entered STN: 18 Oct 1991

TI Process for producing optically active **atenolol** and intermediate thereof

IN Takehira, Yoshikazu; Saragai, Nobuaki; Kitaori, Kazuhiro

PA Daiso Co., Ltd., Japan

SO Eur. Pat. Appl., 14 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM C07C231-18

ICS C07C235-34

ICA C07D303-23

CC 25-7 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)

FAN.CNT 1

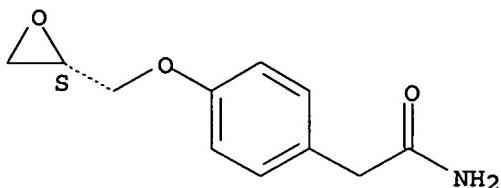
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 435068	A2	19910703	EP 1990-123904	19901212
	EP 435068	A3	19911113		
	EP 435068	B1	19950329		
	R: CH, DE, ES, FR, GB, IT, LI				
	JP 03200753	A2	19910902	JP 1989-344447	19891227
	JP 06074243	B4	19940921		
	US 5130482	A	19920714	US 1990-624302	19901207
	CA 2032098	AA	19910628	CA 1990-2032098	19901212
	CA 2032098	C	19980414		
	EP 605384	A1	19940706	EP 1994-100873	19901212
	EP 605384	B1	19960327		
	R: CH, DE, ES, FR, GB, IT, LI				
	ES 2072960	T3	19950801	ES 1990-123904	19901212

ES 2088299	T3	19960801	ES 1994-100873	19901212
CA 2157938	C	19980714	CA 1990-2157938	19901212
US 5223646	A	19930629	US 1992-871743	19920421
PRAI JP 1989-344447	A	19891227		
US 1990-624302	A3	19901207		
CA 1990-2032098	A3	19901212		
EP 1990-123904	A3	19901212		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 435068	ICM ICS ICA	C07C231-18 C07C235-34 C07D303-23
EP 435068	ECLA	C07C231/18; C07D303/22B
EP 605384	ECLA	C07C231/20; C07C235/46
OS	CASREACT 115:158705; MARPAT 115:158705	
AB	(R)- And (S)-atenolol, p-H <sub>2</sub> NCOCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OCH <sub>2</sub> CH(OH)CH <sub>2</sub> NHCHMe <sub>2</sub> (I) were prepared by treating p-H <sub>2</sub> NCOCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OH with (R)- and (S)-epichlorohydrin followed by treatment of the glycidyl ether with Me <sub>2</sub> CHNH <sub>2</sub> . Thus, p-H <sub>2</sub> NCOCH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OH was treated with (R)-(-)-epichlorohydrin in H <sub>2</sub> O containing NaOH to give the (S)-(+)-glycidyl ether (64%), which was treated with Me <sub>2</sub> CHNH <sub>2</sub> in MeOH to give 89% (S)-(-)-I with 93% ee. I were purified via acid salts.	
ST	atenolol prep; glycidyl ether atenolol intermediate	
IT	136259-68-2P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and neutralization of)	
IT	56715-12-9P 136259-70-6P 136259-71-7P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, with isopropylamine)	
IT	136259-67-1P 136259-69-3P 136259-72-8P 136259-73-9P 136259-74-0P 136259-75-1P 136259-76-2P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of)	
IT	56715-13-0P, (R)-(+)-Atenolol 93379-54-5P, (S)-(-)-Atenolol RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, improved process for)	
IT	51594-55-9, (R)-(-)-Epichlorohydrin, reactions 67843-74-7, (S)-(+)-Epichlorohydrin, reactions RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with (hydroxyphenyl)acetamide)	
IT	17194-82-0 RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with epichlorohydrins)	
IT	75-31-0, Isopropylamine, reactions RL: RCT (Reactant); RACT (Reactant or reagent) (reaction of, with glycidic ethers, in synthesis of atenolol)	
IT	56715-12-9P 136259-70-6P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation and reaction of, with isopropylamine)	
RN	56715-12-9 HCAPLUS	
CN	Benzeneacetamide, 4-[(2S)-oxiranylmethoxy]- (9CI) (CA INDEX NAME)	

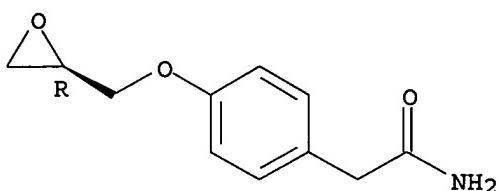
Absolute stereochemistry. Rotation (+).



RN 136259-70-6 HCAPLUS

CN Benzeneacetamide, 4-(oxiranylmethoxy)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 136259-74-0P 136259-76-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 136259-74-0 HCAPLUS

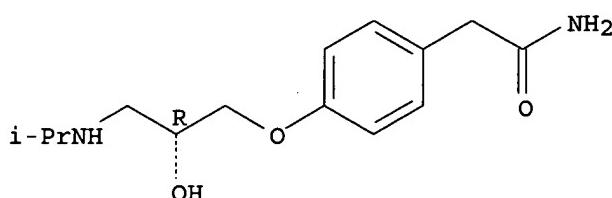
CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]-, (R)-,  
mono(4-methylbenzenesulfonate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 56715-13-0

CMF C14 H22 N2 O3

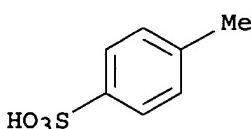
Absolute stereochemistry. Rotation (+).



CM 2

CRN 104-15-4

CMF C7 H8 O3 S

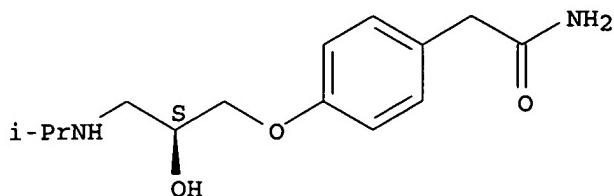


RN 136259-76-2 HCAPLUS

CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]-,

monohydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

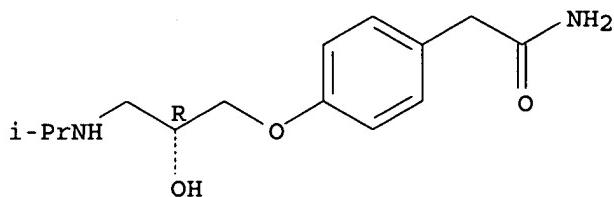
IT 56715-13-0P, (R)-(+)-Atenolol 93379-54-5P,  
(S)-(-)-Atenolol

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, improved process for)

RN 56715-13-0 HCPLUS

CN Benzeneacetamide, 4-[(2R)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
(9CI) (CA INDEX NAME)

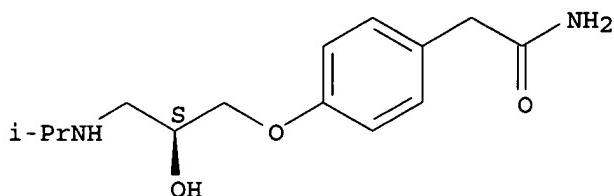
Absolute stereochemistry. Rotation (+).



RN 93379-54-5 HCPLUS

CN Benzeneacetamide, 4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

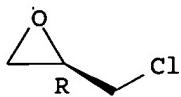


IT 51594-55-9, (R)-(-)-Epichlorohydrin, reactions  
67843-74-7, (S)-(+)-Epichlorohydrin, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with (hydroxyphenyl)acetamide)

RN 51594-55-9 HCPLUS

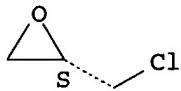
CN Oxirane, (chloromethyl)-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

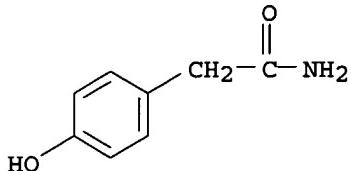


RN 67843-74-7 HCAPLUS  
 CN Oxirane, (chloromethyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 17194-82-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with epichlorohydrins)  
 RN 17194-82-0 HCAPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



L57 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1991:84283 HCAPLUS  
 DN 114:84283  
 ED Entered STN: 09 Mar 1991  
 TI Process for amino alcohol preparation  
 IN Torres Esteban, Josep Maria; Cuixart Grande, Jesus Maria; Campon Pardo, Julio; Ribalta Baro, Miguel  
 PA Sintenovo S. A., Spain; Mefar S. A.  
 SO Span., 4 pp.  
 CODEN: SPXXAD  
 DT Patent  
 LA Spanish  
 IC ICM C07C089-02  
 ICS C07C091-08  
 CC 45-4 (Industrial Organic Chemicals, Leather, Fats, and Waxes)  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI ES 2006944	A6	19890516	ES 1988-1514	19880516
PRAI ES 1988-1514		19880516		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
ES 2006944	ICM C07C089-02	
	ICS C07C091-08	

AB The title process for preparing 1-(4-carbamoylmethylphenoxy)-3-isopropylamino-2-propanol comprises reacting phenol with glyoxylic acid at 60° to 4-hydroxymandalic acid, reducing with hydroiodic acid to 4-hydroxyphenylacetic acid, esterifying and aminating to 4-hydroxyphenylactamide, reacting with epichlorohydrin to

1-(4-carbamoylmethylphenoxy)-2,3-epoxypropane and 1-(4-carbamoylmethylphenoxy)-3-chloro-2-propanol, and reacting with isopropylamine.

ST amino alc prep; carbamoylmethylphenoxyisopropylaminopropanol prepn

IT Alcohols, preparation  
RL: IMF (Industrial manufacture); PREP (Preparation)  
(amino, preparation of)

IT 156-38-7P, 4-Hydroxyphenylacetic acid  
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and esterification and amination of)

IT 17194-82-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, with epichlorohydrin)

IT 29122-69-8P 115538-83-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, with isopropylamine)

IT 1198-84-1P, 4-Hydroxymandelic acid  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and reduction of, by hydroiodic acid)

IT 29122-68-7P  
RL: IMF (Industrial manufacture); PREP (Preparation)  
(preparation of)

IT 75-31-0, Isopropylamine, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with carbamoylmethylphenoxypropane derivative)

IT 108-95-2, Phenol, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with glyoxylic acid)

IT 106-89-8, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with hydroxyphenylactamide)

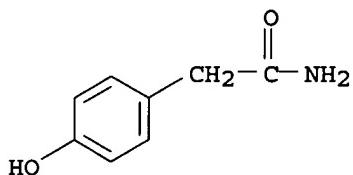
IT 298-12-4, Glyoxylic acid  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with phenol)

IT 10034-85-2, Hydroiodic acid  
RL: USES (Uses)  
(reductant, for hydroxymandelic acid)

IT 17194-82-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, with epichlorohydrin)

RN 17194-82-0 HCAPLUS

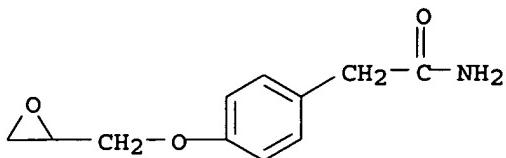
CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



IT 29122-69-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, with isopropylamine)

RN 29122-69-8 HCAPLUS

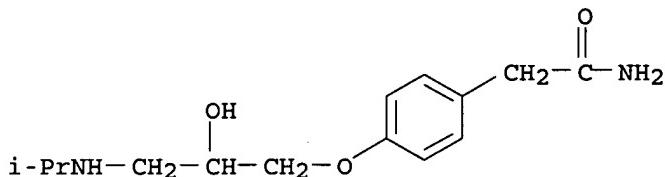
CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P

RL: IMF (Industrial manufacture); PREP (Preparation)  
(preparation of)

RN 29122-68-7 HCAPLUS

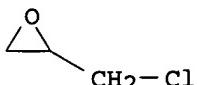
CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
(CA INDEX NAME)

IT 106-89-8, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with hydroxyphenylactamide)

RN 106-89-8 HCAPLUS

CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



L57 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1989:594562 HCAPLUS

DN 111:194562

ED Entered STN: 25 Nov 1989

TI Preparation of aromatic epoxides as intermediates for  $\beta$ -adrenergic blockers

IN Maehara, Kyoshi; Koshigoe, Taichi; Aoki, Shigeru; Tomyoshi, Noriko; Nagao, Susumu

PA Nippon Kayaku Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

IC ICM C07D303-22

ICS B01J031-02; C07D301-00

ICA C07B061-00

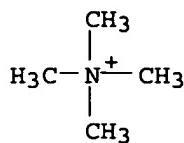
CC 27-2 (Heterocyclic Compounds (One Hetero Atom))  
Section cross-reference(s): 1

FAN.CNT 1

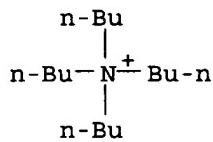
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 01102072	A2	19890419	JP 1987-259481	19871016
PRAI JP 1987-259481		19871016		

CLASS

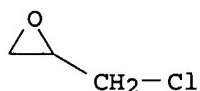
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
<del>JP 01102072</del>	ICM	C07D303-22
	ICS	B01J031-02; C07D301-00
	ICA	C07B061-00
OS	MARPAT 111:194562	
AB	The title compds. ArOX (Ar = aryl; X = glycidyl), useful as intermediate for atenolol, etc., are prepared by treating ArOH with epichlorohydrin in the presence of phase-transfer catalyst RR13N+ X- (R = benzyl, C1-8 alkyl; R1 = C1-4 alkyl; X = halo, sulfate) and then ending the reaction by addition of alkali hydroxides. A mixture of p-hydroxyphenylacetamide, Bu4NBr, and epichlorohydrin was heated at 65-66° for 1 h and treated with KOH-MeOH at 70-72° for 1 h to give 88.5% p-carbamoylmethylphenoxy-2,3-epoxypropane (I), vs., 65.4% using piperidine instead of Bu4NBr. I was treated with isopropylamine in MeOH at 45-50° for 1 h to give atenolol (total yield 75%).	
ST	arom epoxide intermediate adrenergic blocker; oxirane prepn intermediate adrenergic blocker	
IT	Epoxides RL: SPN (Synthetic preparation); PREP (Preparation) (aryl, preparation of, as intermediates for β-adrenergic blockers)	
IT	Etherification catalysts (phase-transfer, quaternary ammonium salts, for aromatic alcs. with epichlorohydrin)	
IT	Quaternary ammonium compounds, uses and miscellaneous RL: CAT (Catalyst use); USES (Uses) (tetraalkyl, halides, phase-transfer catalysts, for etherification of aromatic alcs. with epichlorohydrin)	
IT	Adrenergic antagonists (β-, intermediates for, aromatic epoxides as)	
IT	75-57-0, Tetramethylammonium chloride 1643-19-2, Tetrabutylammonium bromide RL: CAT (Catalyst use); USES (Uses) (catalysts, for etherification of aromatic alcs. with epichlorohydrin)	
IT	106-89-8, reactions RL: RCT (Reactant); RACT (Reactant or reagent) (etherification by, of aromatic alcs.)	
IT	17194-82-0, p-Hydroxyphenylacetamide 56718-71-9 RL: RCT (Reactant); RACT (Reactant or reagent) (etherification of, with epichlorohydrin)	
IT	29122-69-8P, 1-p-Carbamoylmethylphenoxy-2,3-epoxypropane 56718-70-8P RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as intermediate for β-adrenergic blockers)	
IT	29122-68-7P, Atenolol 56392-18-8P, Metoprolol hydrochloride RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as β-adrenergic blocker, aromatic epoxides as intermediates for)	
IT	75-57-0, Tetramethylammonium chloride 1643-19-2, Tetrabutylammonium bromide RL: CAT (Catalyst use); USES (Uses) (catalysts, for etherification of aromatic alcs. with epichlorohydrin)	
RN	75-57-0 HCAPLUS	
CN	Methanaminium, N,N,N-trimethyl-, chloride (9CI) (CA INDEX NAME)	

● Cl<sup>-</sup>

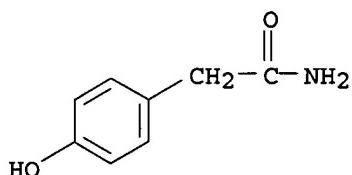
RN 1643-19-2 HCAPLUS  
 CN 1-Butanaminium, N,N,N-tributyl-, bromide (9CI) (CA INDEX NAME)

● Br<sup>-</sup>

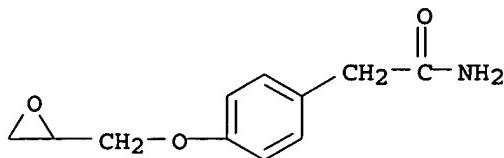
IT 106-89-8, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (etherification by, of aromatic alcs.)  
 RN 106-89-8 HCAPLUS  
 CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



IT 17194-82-0, p-Hydroxyphenylacetamide  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (etherification of, with epichlorohydrin)  
 RN 17194-82-0 HCAPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



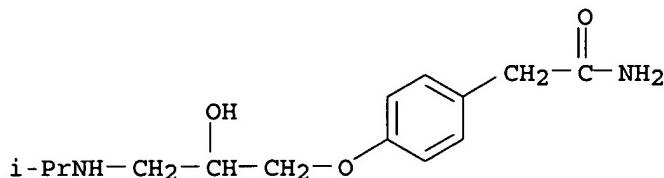
IT 29122-69-8P, 1-p-Carbamoylmethoxy-2,3-epoxypropane  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, as intermediate for β-adrenergic blockers)  
 RN 29122-69-8 HCAPLUS  
 CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P, Atenolol

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as β-adrenergic blocker, aromatic epoxides as  
intermediates for)

RN 29122-68-7 HCAPLUS

CN Benzeneacetamide, 4- [2-hydroxy-3- [(1-methylethyl)amino]propoxy] - (9CI)  
(CA INDEX NAME)

L57 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1987:439429 HCAPLUS

DN 107:39429

ED Entered STN: 08 Aug 1987

TI Process for the preparation of (carbamoylmethylphenoxy)isopropanolamines  
useful as cardiac β-blockersIN Torres Esteban, Josep Maria; Cuixart Grande, Jesus Maria; Juste Sese,  
Rafael

PA Juste S. A. Quimico-Farmaceutica, Spain

SO Span., 10 pp.

CODEN: SPXXAD

DT Patent

LA Spanish

IC ICM C07C089-02

ICS C07C091-04; A61K031-13

CC 25-19 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
Section cross-reference(s): 1

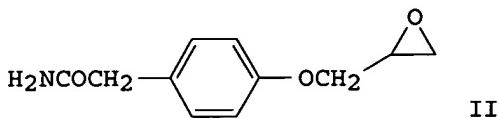
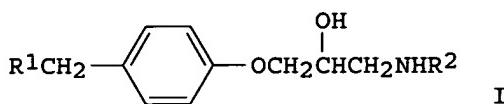
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI ES 539244	A1	19860601	ES 1984-539244	19841229
PRAI ES 1984-539244		19841229		

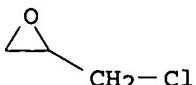
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
ES 539244	ICM	C07C089-02
	ICS	C07C091-04; A61K031-13

GI

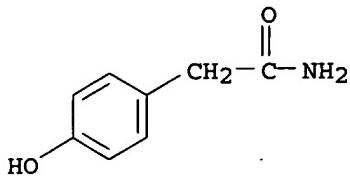


- AB The title compds. [I; R1 = (un)substituted CONH2; R2 = H, Me, Et, Pr, CHMe2, CMe3, etc.], useful as cardiac  $\beta$ -blockers, are prepared Thus, amidation of HO2CCH2C6H4OH-4 via the acid chloride gave 86-88% H2NCOCH2C6H4OH-4, which was alkylated by epichlorohydrin in EtOH containing NaOH to give (carbamoylmethylphenoxy)epoxypropane II. Aminolysis of II by Me2CHNH2 in H2O at 70° gave I (R1 = CONH2, R2 = CHMe2; i.e. atenolol).
- ST carbamoylmethylphenoxyisopropanolamine prepn beta blocker; phenoxyisopropanolamine carbamoylmethyl prepn beta blocker; isopropanolamine carbamoylmethylphenoxy prepn beta blocker; atenolol
- IT 106-89-8, Epichlorohydrin, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (alkylation by, of hydroxyphenylacetamide)
- IT 156-38-7, p-Hydroxyphenylacetic acid  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (amidation of, via acid chloride)
- IT 75-31-0, Isopropylamine, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (aminolysis by, of (carbamoylmethylphenoxy)epoxypropane)
- IT 17194-82-0P, p-Hydroxyphenylacetamide  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and alkylation of, by epichlorohydrin)
- IT 37859-23-7P, p-Hydroxyphenylacetyl chloride  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and amidation of)
- IT 29122-69-8P, 1-(p-Carbamoylmethylphenoxy)-2,3-epoxypropane  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and aminolysis of)
- IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, from hydroxyphenylacetic acid)
- IT 106-89-8, Epichlorohydrin, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (alkylation by, of hydroxyphenylacetamide)
- RN 106-89-8 HCPLUS
- CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)

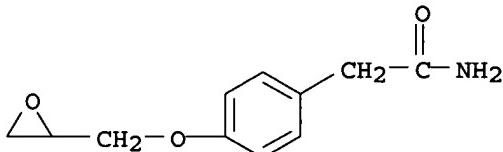


- IT 17194-82-0P, p-Hydroxyphenylacetamide  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)

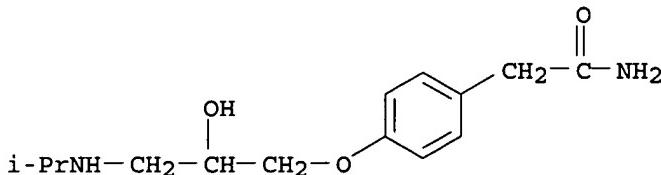
(preparation and alkylation of, by epichlorohydrin)  
 RN 17194-82-0 HCPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



IT 29122-69-8P, 1-(p-Carbamoylmethylphenoxy)-2,3-epoxypropane  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and aminolysis of)  
 RN 29122-69-8 HCPLUS  
 CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P, Atenolol  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of, from hydroxyphenylacetic acid)  
 RN 29122-68-7 HCPLUS  
 CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)



L57 ANSWER 16 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN  
 AN 1983:504960 HCPLUS  
 DN 99:104960  
 ED Entered STN: 12 May 1984  
 TI 2-[P-[2-Hydroxy-3-(isopropylamino)propoxy]phenyl]acetamide  
 IN Vallas Rodoreda, Enrique  
 PA Spain  
 SO Span., 7 pp.  
 CODEN: SPXXAD  
 DT Patent  
 LA Spanish  
 IC C07C103-26; A61K031-165  
 CC 25-10 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI ES 509814	A1 19830201	ES 1982-509814	19820223
PRAI ES 1982-509814		19820223	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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ES 509814	IC C07C103-26IC	A61K031-165
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AB The title compound (I) was prepared from 4-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CONH<sub>2</sub> (II); I is useful as a β-adrenergic blocking agent (no data). II was treated with epichlorohydrin and K<sub>2</sub>CO<sub>3</sub> to yield a glycidyl ether, and the product was heated with Me<sub>2</sub>CHNH<sub>2</sub> in Et<sub>2</sub>O to give I.

ST phenoxyisopropanolamine prepn adrenergic blocker

IT Sympatholytics  
(β-, phenoxyisopropanolamine derivative)

IT 106-89-8, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification by, of phenol derivative)

IT 17194-82-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification of, by epichlorohydrin)

IT 29122-69-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and ring cleavage of, by isopropylamine)

IT 29122-68-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

IT 75-31-0, reactions

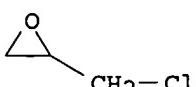
RL: RCT (Reactant); RACT (Reactant or reagent)  
(ring cleavage by, of glycidyl (carbamoylmethyl)phenyl ether)

IT 106-89-8, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification by, of phenol derivative)

RN 106-89-8 HCPLUS

CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)

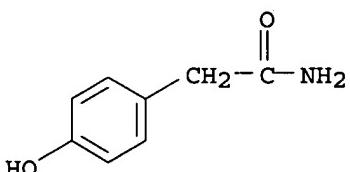


IT 17194-82-0

RL: RCT (Reactant); RACT (Reactant or reagent)  
(etherification of, by epichlorohydrin)

RN 17194-82-0 HCPLUS

CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)

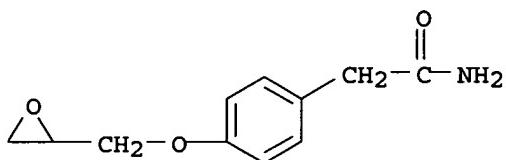


IT 29122-69-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and ring cleavage of, by isopropylamine)

RN 29122-69-8 HCPLUS

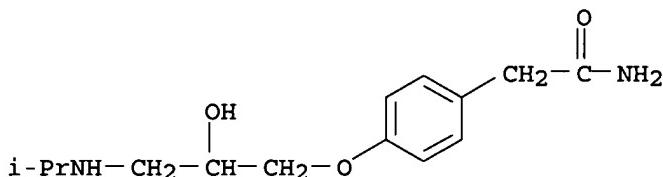
CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 29122-68-7 HCAPLUS

CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
(CA INDEX NAME)

L57 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1982:154993 HCAPLUS

DN 96:154993

ED Entered STN: 12 May 1984

TI Studies on the metabolism of atenolol. Characterization and determination of a new urinary metabolite in the rat

AU Matsuki, Yasuhiko; Ito, Tomiharu; Komatsu, Sakae; Nambara, Toshio

CS Food Drug Saf. Cent., Hatano Res. Inst., Kanagawa, 257, Japan

SO Chemical &amp; Pharmaceutical Bulletin (1982), 30(1), 196-201

CODEN: CPBTAL; ISSN: 0009-2363

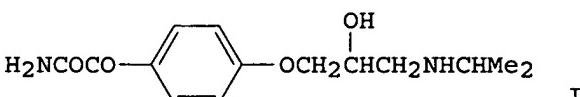
DT Journal

LA English

CC 1-2 (Pharmacology)

Section cross-reference(s) : 25

GI



- AB A new urinary metabolite of atenolol [29122-68-7] in the rat was characterized and isolated. The metabolite, 4-(2-hydroxy-3-isopropylaminopropoxy)phenylglyoxylic acid amide (I) [74908-93-3], represented 1.04% of the total dose of atenolol administered. A gas chromatog. method for the determination of I in urine is presented.
- ST atenolol metabolite urine; gas chromatog atenolol metabolite urine
- IT Urine analysis  
(atenolol metabolite determination in, by gas chromatog.)

IT 29122-68-7  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (metabolism of, urinary metabolite determination in)

IT 68758-68-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (oxidation of)

IT 70080-54-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and amidation of)

IT 74908-93-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and determination of, in urine, as atenolol metabolite)

IT 81346-71-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction with acetone)

IT 81346-70-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reaction with isopropylamine)

IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reductive amination of)

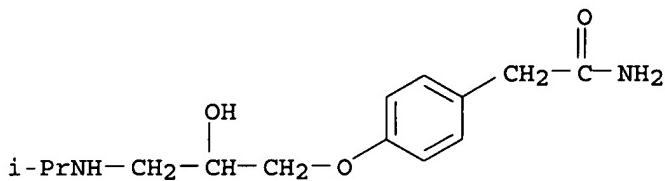
IT 81346-72-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT 17194-82-0 81346-69-2  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with epichlorohydrin)

IT 29122-68-7  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (metabolism of, urinary metabolite determination in)

RN 29122-68-7 HCPLUS

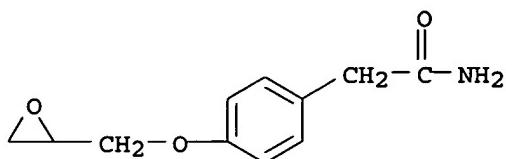
CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)



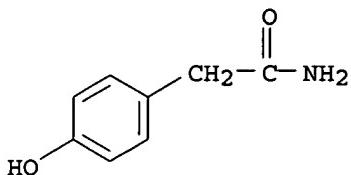
IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and reductive amination of)

RN 29122-69-8 HCPLUS

CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 17194-82-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with epichlorohydrin)  
 RN 17194-82-0 HCPLUS  
 CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



L57 ANSWER 18 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN  
 AN 1980:180847 HCPLUS  
 DN 92:180847  
 ED Entered STN: 12 May 1984  
 TI p-Hydroxybenzyl cyanide and p-(2-hydroxy-3-isopropylaminopropoxy)phenylacetamide  
 PA Imperial Chemical Industries Ltd., UK  
 SO Jpn. Kokai Tokkyo Koho, 2 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 IC C07C103-26; C07C121-75; C07C102-00; C07C120-00  
 CC 25-20 (Noncondensed Aromatic Compounds)

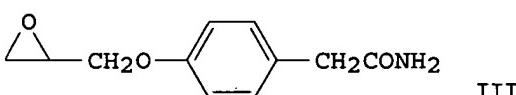
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 54148744	A2	19791121	JP 1978-57487	19780515
PRAI JP 1978-57487	A	19780515		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES		
JP 54148744	IC	C07C103-26IC	C07C121-75IC	C07C102-00IC
		C07C120-00		

GI



III

AB p-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CN (I) was prepared by treating p-HOC<sub>6</sub>H<sub>4</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H (II) with alkali metal cyanides in DMF, Me<sub>2</sub>SO, or 2-pyrrolidone at 120-190°. Hydrolyzing I gave p-HOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CONH<sub>2</sub>, which was treated with epichlorohydrin to give III. Aminating III with Me<sub>2</sub>CHNH<sub>2</sub> gave p-Me<sub>2</sub>CHNHCH<sub>2</sub>CH(OH)CH<sub>2</sub>OCC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CONH<sub>2</sub>. Thus, heating 10 g II, NaCN,

NaOH, and DMF 1 h at 130° gave 80% I.

ST hydroxybenzyl cyanide; hydroxyisopropylaminopropoxyphenylacetamide; acetamide hydroxyisopropylaminopropoxyphenyl; cyanation phenylglycine; glycine phenyl cyanation

IT Cyanation  
(of phenylglycine, phenylacetonitrile from)

IT 143-33-9 151-50-8  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyanation of phenylglycine by, phenylacetonitrile from)

IT 938-97-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(cyanation of, hydroxyphenylacetonitrile from)

IT 29122-69-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and amination of)

IT 14191-95-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(preparation and hydrolysis of)

IT 17194-82-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and reaction with epichlorohydrin)

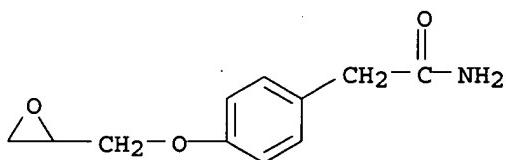
IT 29122-68-7P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

IT 106-89-8, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with hydroxyphenylacetamide)

IT 29122-69-8P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and amination of)

RN 29122-69-8 HCAPLUS

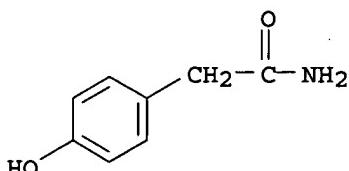
CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 17194-82-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
(Preparation); RACT (Reactant or reagent)  
(preparation and reaction with epichlorohydrin)

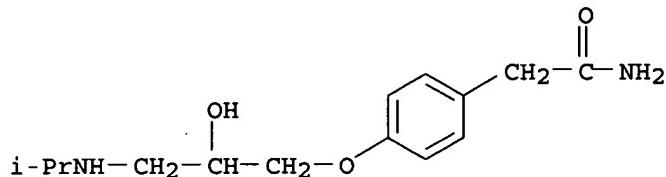
RN 17194-82-0 HCAPLUS

CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)

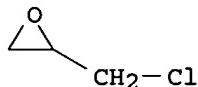


IT 29122-68-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)  
 RN 29122-68-7 HCPLUS  
 CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)



IT 106-89-8, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with hydroxyphenylacetamide)  
 RN 106-89-8 HCPLUS  
 CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



L57 ANSWER 19 OF 19 HCPLUS COPYRIGHT 2005 ACS on STN  
 AN 1978:104956 HCPLUS  
 DN 88:104956  
 ED Entered STN: 12 May 1984  
 TI Phenylacetamide derivative  
 IN Juste Sese, Rafael  
 PA Juste S. A. Quimico-Farmaceutica, Spain  
 SO Span., 7 pp.  
 CODEN: SPXXAD  
 DT Patent  
 LA Spanish  
 IC C07C  
 CC 25-19 (Noncondensed Aromatic Compounds)  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI ES 449244	A1	19770801	ES 1976-449244	19760625
PRAI ES 1976-449244	A1	19760625		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
ES 449244	IC	C07C

AB 4-[Me2CHNHCH2CH(OH)CH2O]C6H4CH2CONH2 (I) was prepared in 4 steps from 4-HOC6H4CO2H, i.e., esterification with MeOH, ammonolysis with aqueous NH4OH, etherification with epichlorohydrin, and cleavage of the oxirane ring with excess (50 mol parts) Me2CHNH2. I has  $\beta$ -adrenergic blocking activity and is an antihypertensive agent (no data).

ST phenylacetamide aminohydroxypropoxy; sympatholytic phenylacetamide; antihypertensive phenylacetamide

IT Antihypertensives  
 (4-[3-(isopropylamino)-2-hydroxypropoxy]phenylacetamide as)

IT Sympatholytics  
 ( $\beta$ -, 4-[3-(isopropylamino)-2-hydroxypropoxy]phenylacetamide as)

IT 156-38-7

IT 14199-15-6P  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (esterification of, with methanol)

IT 17194-82-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation and ammonolysis of)

IT 29122-68-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, with epichlorohydrin)

IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, with isopropylamine)

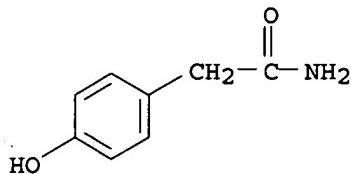
IT 106-89-8, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with (hydroxyphenyl)acetamide)

IT 75-31-0, reactions  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with oxirane derivative)

IT 17194-82-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, with epichlorohydrin)

RN 17194-82-0 HCPLUS

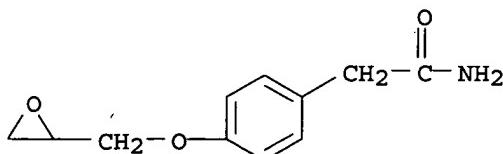
CN Benzeneacetamide, 4-hydroxy- (9CI) (CA INDEX NAME)



IT 29122-69-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP  
 (Preparation); RACT (Reactant or reagent)  
 (preparation and reaction of, with isopropylamine)

RN 29122-69-8 HCPLUS

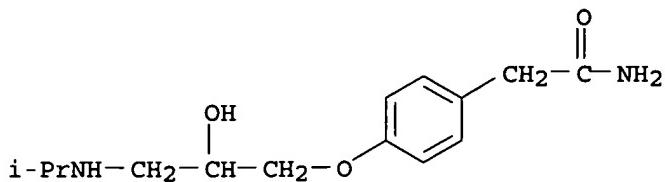
CN Benzeneacetamide, 4-(oxiranylmethoxy)- (9CI) (CA INDEX NAME)



IT 29122-68-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

RN 29122-68-7 HCPLUS

CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI)  
 (CA INDEX NAME)

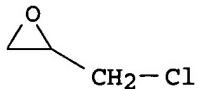


IT 106-89-8, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with (hydroxyphenyl)acetamide)

RN 106-89-8 HCAPLUS

CN Oxirane, (chloromethyl)- (9CI) (CA INDEX NAME)



=&gt; =&gt; d his

(FILE 'HOME' ENTERED AT 10:17:04 ON 11 JAN 2005)  
SET COST OFFFILE 'REGISTRY' ENTERED AT 10:17:10 ON 11 JAN 2005  
E ATENOLOL/CN

L1 1 S E3  
E C14H22N2O3/MF

L2 342 S E3 AND 46.150.18/RID AND 1/NR

L3 18 S L2 AND BENZENEACETAMIDE

L4 12 S L3 AND 2 HYDROXY

L5 11 S L4 AND PROPOXY

L6 7 S L5 AND 4

L7 3 S L6 NOT (D/ELS OR 11C#)

L8 3 S L2 AND ATENOLOL

L9 3 S L1,L7,L8  
SEL RN

L10 37 S E1-E3/CRN

L11 10 S L10 NOT (MXS/CI OR COMPD OR WITH)  
E EPICHLOROHYDRIN/CN

L12 1 S E3  
E C3H5CLO/MF

L13 23 S E3 AND OC2/ES  
SEL RN 12 17 23

L14 3 S E1-E3

L15 3 S L12,L14  
E C11H13NO3/MF

L16 55 S E3 AND 46.150.18/RID AND OC2/ES AND 2/NR

L17 17 S L16 AND 4

L18 5 S L17 AND BENZENEACETAMIDE

L19 3 S L18 NOT D/ELS  
E C8H9NO2/MF

L20 392 S E3 AND 46.150.18/RID AND 1/NR

L21 147 S L20 AND 4

L22 1 S L21 AND BENZENEACETAMIDE

L23 9 S L20 AND BENZENEACETAMIDE

L24 2 S (SODIUM HYDROXIDE OR POTASSIUM HYDROXIDE)/CN

FILE 'HCAPLUS' ENTERED AT 11:12:24 ON 11 JAN 2005

L25 116 S L22  
 L26 15885 S L15  
 L27 32010 S EPICHLOROHYDRIN?  
 L28 35012 S L26,L27  
 L29 58 S L19  
 L30 3162 S L9 OR L11  
 L31 4161 S ATENOLOL  
 L32 4406 S L30,L31  
 L33 19 S L25 AND L28 AND L29 AND L32  
 L34 6 S L33 AND (L24 OR NAOH OR KOH OR (NA OR K OR SODIUM OR POTASSIU  
 L35 1 S L33 AND (QUAT? (L)AMMON?)  
 L36 6 S L34,L35  
 L37 105 S L30 (L) PREP+NT/RL  
 L38 18 S L33 AND L37  
 L39 8366 S (L22 OR L28 OR L19) (L)RACT+NT/RL  
 L40 920 S (L22 OR L28 OR L19) (L)CAT/RL  
 L41 18 S L38 AND L39,L40  
 L42 6 S L36 AND L41  
 L43 13 S L33-L36,L38,L41 NOT L42  
 L44 19 S L42,L43  
 SEL RN

## FILE 'REGISTRY' ENTERED AT 11:17:17 ON 11 JAN 2005

L45 116 S E1-E116  
 L46 1 S L45 AND L22  
 L47 3 S L45 AND L15  
 L48 3 S L45 AND L19  
 L49 5 S L45 AND L9,L11  
 L50 104 S L45 NOT L46-L49  
 L51 3 S L50 AND IUM  
 L52 3 S L50 AND N N N  
 L53 3 S L50 AND N N  
 L54 3 S L51-L53  
 L55 1 S L45 AND L24

## FILE 'HCAPLUS' ENTERED AT 11:19:16 ON 11 JAN 2005

L56 2 S L54 AND L44  
 L57 19 S L44,L56

## FILE 'HCAPLUS' ENTERED AT 11:19:39 ON 11 JAN 2005

E MEHTA S/AU  
 L58 189 S E3,E18  
 L59 2 S E51  
 E SATISH/AU  
 L60 1 S E32  
 E RAMANLAL/AU  
 E BHAWAL B/AU  
 L61 84 S E3,E4,E8,E9  
 E BABURAO/AU  
 E MANIKROA/AU  
 E DESHPANDE/AU  
 E DESHPANDE V/AU  
 L62 77 S E3,E8  
 E DESHPANDE VISH/AU  
 L63 22 S E4,E5  
 E VISHNU/AU  
 L64 58 S E3  
 E HARI/AU  
 L65 2 S E26  
 L66 27 S E121  
 E GURJAR /AU  
 L67 123 S E22-E25  
 E MUKUND/AU

L68 1 S E5  
E KESHAV/AU  
L69 586 S L58-L68  
L70 0 S L69 AND L32  
L71 41 S L69 AND P/DT  
L72 7 S L69 AND L22,L15,L19  
L73 5 S L71 AND L72  
L74 2 S L72 NOT L73  
L75 0 S L58-L60 AND L61-L68  
L76 0 S L61 AND L62-L68  
L77 0 S L62-L66 AND L67,L68  
E IN2003-1148/AP, PRN  
E IN2003-MU1148/AP, PRN  
E IN2003-MUM1148/AP, PRN  
SET COST ON

&gt;

FILE 'HOME' ENTERED AT 08:53:58 ON 11 JAN 2005

=> file casreact  
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CASREACT' ENTERED AT 08:54:22 ON 11 JAN 2005  
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT  
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 9 Jan 2005 VOL 142 ISS 2

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\*  
\* CASREACT now has more than 8 million reactions  
\*  
\*\*\*\*\*

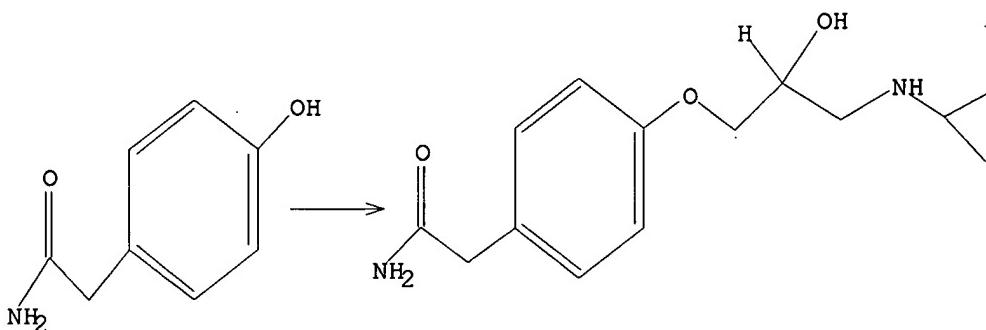
Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>  
Uploading C:\STNEXP4\10701902.str

## L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS  
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 08:54:44 FILE 'CASREACT'  
SCREENING COMPLETE - 3 REACTIONS TO VERIFY FROM 1 DOCUMENTS

100.0% DONE 3 VERIFIED 0 HIT RXNS 0 DOCS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED VERIFICATIONS: 3 TO 163  
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1 ( 0 REACTIONS)

=> s 11 ful  
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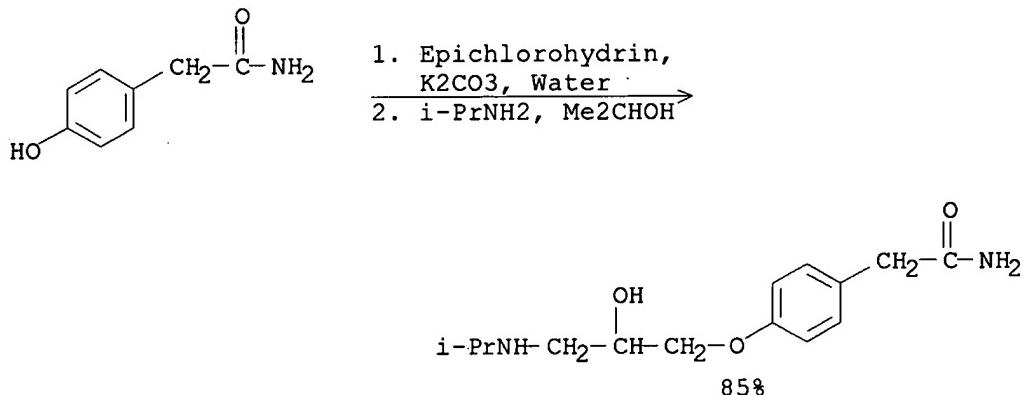
100.0% DONE 129 VERIFIED 11 HIT RXNS 6 DOCS  
SEARCH TIME: 00.00.01

L3 6 SEA SSS FUL L1 ( 11 REACTIONS)

=> d 13 1-6

L3 ANSWER 1 OF 6 CASREACT COPYRIGHT 2005 ACS on STN

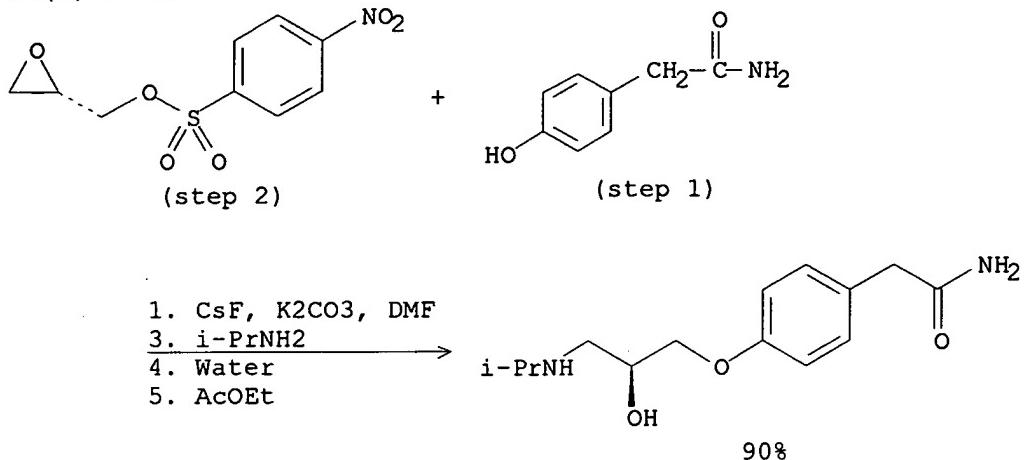
RX(13) OF 28 - 2 STEPS



REF: Huaihai Gongxueyuan Xuebao, 9(2), 36-38; 2000

L3 ANSWER 2 OF 6 CASREACT COPYRIGHT 2005 ACS on STN

RX(2) OF 20

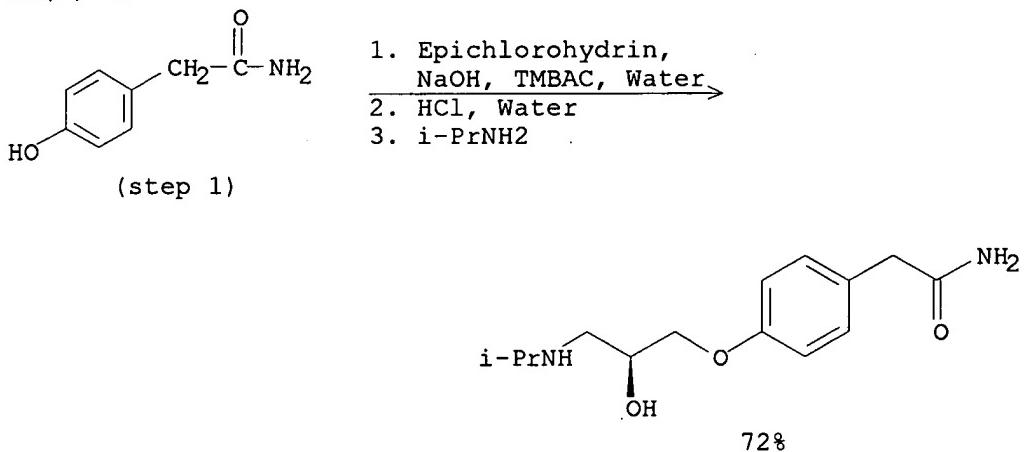


REF: Tetrahedron, 55(50), 14381-14390; 1999

NOTE: STEREOSELECTIVE

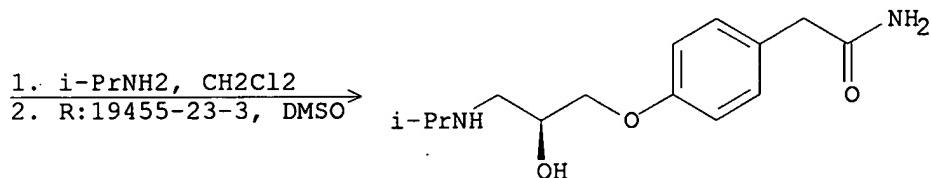
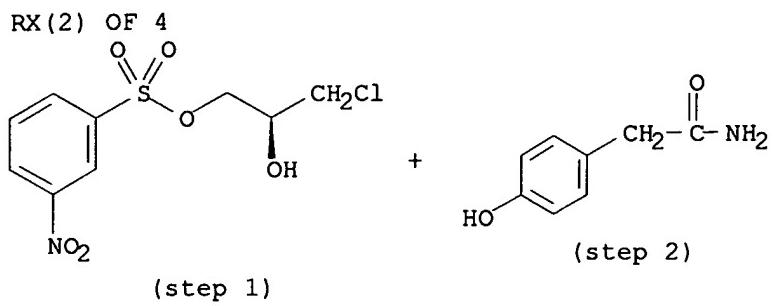
L3 ANSWER 3 OF 6 CASREACT COPYRIGHT 2005 ACS on STN

RX(1) OF 7



REF: Jpn. Kokai Tokkyo Koho, 04198175, 17 Jul 1992, Heisei

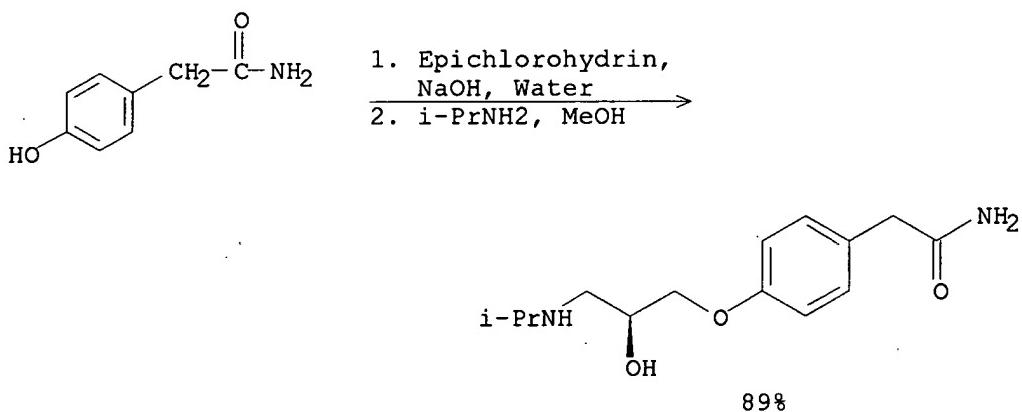
L3 ANSWER 4 OF 6 CASREACT COPYRIGHT 2005 ACS on STN



REF: PCT Int. Appl., 9110642, 25 Jul 1991  
NOTE: stereoselective

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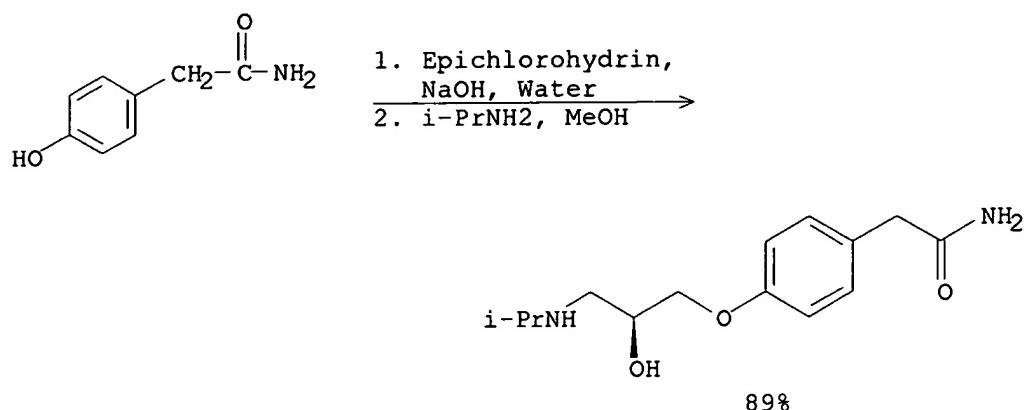
RX(3) OF 3 - 2 STEPS



REF: Jpn. Kokai Tokkyo Koho, 03077856, 03 Apr 1991, Heisei

L3 ANSWER 6 OF 6 CASREACT COPYRIGHT 2005 ACS on STN

RX(6) OF 8 - 2 STEPS



REF: Eur. Pat. Appl., 435068, 03 Jul 1991